821R95019

Development Document For Proposed Effluent Limitations Guidelines and Standards For The Pharmaceutical Manufacturing Point Source Category

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February 28, 1995

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ACKNOWLEDGEMENTS

The Agency wishes to acknowledge many important contributions to this project.

The development of the proposed effluent guidelines was led by the Commodities Branch of the Engineering and Analysis Division (EAD) of the Office of Science and Technology (OST). Mr. Thomas O'Farrell and Ms. Sheila Frace, Director and Deputy Director of EAD, respectively, provided the leadership and management support to complete the proposed rule within the court-ordered schedule. Mr. Robert Perciasepe and Ms. Dana Minerva, Assistant Administrator and Deputy Assistant Administrator, respectively, of the Office of Water, and Mr. Tudor Davies, Director of the Office of Science and Technology, provided senior management support that was critical to the successful completion of this effort. A number of EAD staff made major contributions to the proposed effluent guidelines. Dr. Frank H. Hund served as the Project Officer and Mr. Edward Terry served as Assistant Project Officer. Mr. Donald Anderson provided technical direction and coordination with the Office of Air Quality Planning and Standards and the Office of Solid Waste. Ms. Debra Nicoll (in the early stages of the project), Mr. Joe Ford and Mr. George Zipf (both formerly of EPA), Mr. William Anderson, Dr. Henry D. Kahn, and Mr. Neil Patel all contributed to the economic and regulatory impact analyses, and to the statistical analyses supporting development of the effluent limitations. Mr. Ryan Childs (formerly of EPA), Mr. Ed Gardetto, and Mr. Richard Healy (Standards and Applied Science Division) provided direction to the environmental assessment and benefits analysis. Ms. CarolAnn Siciliano (in the final stages of the project), Mr. Brian Grant, Ms. Carrie Wehling, and Ms. Susan Lepow of the Office of General Counsel provided extensive legal support and guidance. Dr. William A. Telliard provided support for laboratory analyses and analytical methods development. Mr. Steve Geil of the Office of Wastewater Management, Permits Division, assisted with implementation aspects of this proposal. Administrative and word processing support were provided by Ms. Cassandra Holmes and Ms. Dottie Gross without whose tireless efforts these products could not have been completed.

A number of managers and staff in the Office of Air Quality Planning and Standards made significant contributions to this effort, including Mr. Randy McDonald and Ms. Susan Wyatt of the Organic Chemicals Group, Mr. K. C. Hustvedt of the Waste and Chemical Processes Group, Mr. Bruce Jordan, Director of the Emission Standards Division, and Mr. John Seitz, Director of the Office of Air Quality Planning and Standards.

Mr. Glenn Shaul and Mr. Tom Holdsworth, Risk Reduction Engineering Laboratory, Cincinnati, and management of the Office of Research and Development (ORD) contributed significantly during this effort. This contribution included the resources and technical direction necessary to conduct pilot and full scale studies of steam stripping and distillation technology, and an activated sludge biological treatment system enhanced by powdered activated carbon. Data from these studies were critical in developing technology options and performance data used in establishing the proposed effluent limitations.

Staff contributions of a number of other EPA offices were important to this effort, including: Ms. Chantale Wong (formerly of EPA) of the Office of the Administrator; Mr. Richard Kinch and Ms. Lisa Jones of the Office of Solid Waste; and Mr. Nick Bouwes and Ms. Jocelyn Siegel (formerly of EPA) of the Office of Pollution Prevention and Toxics.

EPA wishes to acknowledge the major contributions to this project by the Radian Corporation under EPA Contract No. 68-C0-0032. Staff of Radian Corporation's Herndon, Virginia office, performed many tasks with the Agency's direction that were vital to the successful completion of this rulemaking within the court-ordered schedule, including: collecting and compiling data from the detailed questionnaire, pilot and full scale treatability studies and many other sources; performing engineering analyses and costing of wastewater control and treatment technologies; preparing the engineering and technical inputs to a number of other efforts and contractors supporting this rulemaking; and assisting in preparing this Development Document and the record (including the public docket) supporting this rulemaking. Among the other contractors that provided

assistance to this effort under the Agency's direction were: technical - ABB Environmental Services (formerly E.C. Jordan, Co., during early stages of this project), and Radian Corporation (Milwaukee office - ORD treatability studies); statistical - Science Applications International Corporation (SAIC); economic - Eastern Research Group (ERG), and Research Triangle Institute (during early stages of this project); environmental - Tetra Tech, and Versar (during early stages of this project); and analytical - DynCorp/Viar.

The Agency also wishes to acknowledge the contributions of the Pharmaceutical Research and Manufacturers of America (PhRMA - formerly PMA) and its members. The Agency also acknowledges the extensive contributions made by a large number of companies and employees in responding to the detailed questionnaire and follow-up requests, and graciously opening their plants to numerous visits by EPA and contractor personnel. The data gathered through these efforts were major contributions to the information and data which support this proposed rulemaking.

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SECTION 1

INTRODUCTION

1.1 Legal Authority

The Pharmaceutical Manufacturing Point Source Category Effluent Limitations Guidelines and Standards are being proposed under the authority of Sections 301, 304, 306, 307, 308, and 501 of the Clean Water Act (the Federal Water Pollution Control Act Amendments of 1972, 33 U.S.C. 1251 et seq., as amended by the Clean Water Act of 1977, Pub. L. 95-217, and the Water Quality Act of 1987, Pub. L. 100-4), also referred to as "the Act."

1.2 Background

1.2.1 Clean Water Act

The Federal Water Pollution Control Act Amendments of 1972 established a comprehensive program to "restore and maintain the chemical, physical, and biological integrity of the Nation's waters" (Section 101(a)). To implement the Act, EPA is to issue effluent limitations guidelines, pretreatment standards, and new source performance standards for industrial dischargers.

These guidelines and standards are summarized briefly below:

1. Best Practicable Control Technology Currently Available (BPT) (Section 304(b)(1) of the Act).

   BPT effluent limitations guidelines are generally based on the average of the best existing performance by plants of various sizes, ages, and unit processes within the category or subcategory for control of pollutants.

In establishing BPT effluent limitations guidelines, EPA considers the total cost of achieving effluent reductions in relation to the effluent reduction benefits, the age of equipment and facilities involved, the processes used, process changes required, engineering aspects of the control technologies, nonwater quality environmental impacts, and other factors as the EPA Administrator deems appropriate (Section 304(b)(1)(B) of the Act). The Agency considers the category- or subcategory-wide cost of applying the technology in relation to the effluent reduction benefits. Where existing performance is uniformly inadequate, BPT may be transferred from a different subcategory or category.

2. Best Available Technology Economically Achievable (BAT) (Sections 304(b)(2)(B) and 307(a)(2) of the Act).

In general, BAT effluent limitations guidelines represent the best existing economically achievable performance of plants in the industrial subcategory or category. The Act establishes BAT as the principal national means of controlling the direct discharge of priority pollutants and nonconventional pollutants to waters of the United States. The factors considered in assessing BAT include the age of equipment and facilities involved, the process used, potential process changes, and nonwater quality environmental impacts (Section 304(b)(2)(B)). The Agency retains considerable discretion in assigning the weight to be accorded these factors. As with BPT, where existing performance is uniformly inadequate, BAT may be transferred from a different subcategory or category. BAT may include process changes or internal controls, even when these technologies are not common industry practice.

3. Best Conventional Pollutant Control Technology (BCT) (Section 304(a)(4) of the Act).

The 1977 Amendments added Section 301(b)(2)(E) to the Act establishing BCT for discharges of conventional pollutants from existing industrial point sources. Section 304(a)(4) designated the following as conventional pollutants: biochemical oxygen demand (BOD), total suspended solids (TSS), fecal coliform, pH, and any additional pollutants defined by the Administrator as conventional. The Administrator designated oil and grease as an additional conventional pollutant on July 30, 1979 (44 FR 44501).

BCT is not an additional limitation, but replaces BAT for the control of conventional pollutants. In addition to other factors specified in Section 304(b)(4)(B), the Act requires that BCT limitations be established in light of a two-part "cost-reasonableness" test [American Paper Institute v. EPA,

660 F.2d 954 (4th Cir. 1981)]. EPA must find that proposed BCT limitations are "reasonable" under both tests before establishing them as BCT. If the candidate BCT technology does not pass both tests, BCT is established equal to BPT. In no case may BCT be less stringent than BPT. EPA's current methodology for the general development of BCT limitations was issued in 1986 (51 FR 24974, July 9, 1986).

4. New Source Performance Standards (NSPS) (Section 306 of the Act).

NSPS are based on the best available demonstrated treatment technology. New plants have the opportunity to install the best and most efficient production processes and wastewater treatment technologies. As a result, NSPS should represent the most stringent numerical values attainable through the application of the best available control technology for all pollutants (i.e., conventional, nonconventional, and priority pollutants). In establishing NSPS, EPA is directed to take into consideration the cost of achieving the effluent reduction and any nonwater quality environmental impacts.

5. Pretreatment Standards for Existing Sources (PSES) (Section 307(b) of the Act).

PSES are designed to prevent the discharge of pollutants that pass through, interfere with, or are otherwise incompatible with the operation of publicly owned treatment works (POTWs). The Act requires pretreatment standards for pollutants that pass through POTWs or interfere with POTWs' treatment processes or sludge disposal methods. The legislative history of the 1977 Act indicates that pretreatment standards are to be technology-based and analogous to the BAT effluent limitations guidelines for removal of priority and nonconventional pollutants. For the purpose of determining whether to promulgate national category-wide pretreatment standards, EPA generally determines that there is pass-through of a pollutant and thus a need for categorical standards if the nation-wide average percentage of a pollutant removed by well-operated POTWs achieving secondary treatment is less than the percentage removed by the BAT model treatment system. EPA also determines that there is pass-through of a pollutant if the pollutant exhibits significant volatilization prior to treatment by POTWs. The transfer of the pollutant to another media (air) through volatilization does not constitute treatment.

The General Pretreatment Regulations, which set forth the framework for the implementation of categorical pretreatment standards, are found at 40 CFR Part 403. (Those regulations contain a definition of pass-through that addresses localized rather than national instances of pass-through and does

not use the percent removal comparison test described above. See 52 FR 1586, January 14, 1987.)

6. Pretreatment Standards for New Sources (PSNS) (Section 307(b) of the Act).

Like PSES, PSNS are designed to prevent the discharges of pollutants that pass through, interfere with, or are otherwise incompatible with the operation of POTWs. PSNS are to be issued at the same time as NSPS. New indirect dischargers, like the new direct dischargers, have the opportunity to incorporate into their plants the best available demonstrated technologies. The Agency considers the same factors in promulgating PSNS that it considers in promulgating NSPS.

1.2.2 Section 304(m) Requirements

Section 304(m) of the Clean Water Act (33 U.S.C. 1314(m)), added by the Water Quality Act of 1987, requires EPA to establish schedules for (i) reviewing and revising existing effluent limitations guidelines and standards ("effluent guidelines"), and (ii) promulgating new effluent guidelines. On January 2, 1990, EPA published an Effluent Guidelines Plan (55 FR 80), in which schedules were established for developing new and revised effluent guidelines for several industrial categories. In this notice, the Agency identified the Pharmaceutical Manufacturing Point Source Category as requiring revisions to existing guidelines and identified an estimated schedule for regulatory action.

Natural Resources Defense Council, Inc. (NRDC) and Public Citizen, Inc., challenged the Effluent Guidelines Plan in a suit filed in U.S. District Court for the District of Columbia (NRDC et al. v. Reilly, Civ. No. 89-2980). The plaintiffs charged that EPA's plan did not meet the requirements of Section 304(m). A Consent Decree in this litigation was entered by the Court on January 31, 1992. The Decree required, among other things, that EPA propose revised effluent guidelines for the Pharmaceutical Manufacturing Point Source Category. On May 7, 1992, and May 18, 1994, EPA published updated Effluent Guidelines Biennial Plans (57 FR 19748) and (59 FR 25859), in which schedules were established for developing new and revised effluent guidelines

for several industrial categories, including the Pharmaceutical Manufacturing Point Source Category. The May 18, 1994 plan states that EPA plans to propose effluent guidelines for the Pharmaceutical Manufacturing Point Source Category by August 1994, and take final action by February 1996. Subsequent discussions between EPA and the plantiffs resulted in a revised proposal date of February 1995 and a revised promulgation date of August 1996.

1.2.3 Pollution Prevention Act

In the Pollution Prevention Act of 1990 (42 U.S.C. 13101 et seq., Pub. Law 101-508, November 5, 1990), Congress declared pollution prevention the national policy of the United States. The Act declares that pollution should be prevented or reduced whenever feasible; pollution that cannot be prevented should be recycled or reused in an environmentally safe manner wherever feasible; pollution that cannot be recycled should be treated; and disposal or release into the environment should be chosen only as a last resort.

1.2.4 Prior Regulation of the Pharmaceutical Manufacturing Category

EPA promulgated interim final BPT for the Pharmaceutical Manufacturing Point Source Category on November 17, 1976 (41 FR 50676; 40 CFR Part 439 Subparts A - E). The BPT effluent guidelines established limitations for BOD_5, chemical oxygen demand (COD), TSS, and pH for wastewaters discharged by the extraction, the mixing/ compounding and formulation, and the research subcategories and limitations for BOD_5, COD, and pH for wastewaters discharged by the fermentation and the chemical synthesis subcategories.

On November 26, 1982, EPA proposed regulations applicable to the Pharmaceutical Manufacturing Point Source Category (47 FR 53584) which proposed to modify and expand upon the November 17, 1976 regulations. EPA proposed the following:

- To modify the existing BPT TSS effluent limitations guidelines for the extraction, mixing, compounding and formulating, and research subcategories;

- To extend these revised BPT TSS effluent limitations guidelines to the fermentation and chemical synthesis subcategories;

- To modify the existing BPT COD effluent limitations guidelines for the fermentation, extraction, chemical synthesis, mixing/ compounding and formulation, and research subcategories;

- To propose BPT cyanide effluent limitations guidelines for the fermentation, extraction, chemical synthesis, and mixing/compounding and formulation subcategories;

- To propose BAT COD and cyanide effluent limitations guidelines for the fermentation, extraction, chemical synthesis, and mixing/compounding and formulation subcategories;

- To propose BCT BOD_5, TSS and pH effluent limitations guidelines for the fermentation, extraction, chemical synthesis, and mixing/compounding and formulation subcategories;

- To propose BOD_5, COD, TSS, cyanide and pH NSPS for the fermentation, extraction, chemical synthesis, and mixing/compounding and formulation subcategories; and

- To propose cyanide PSES and PSNS for the fermentation, extraction, chemical synthesis, and mixing/compounding and formulation subcategories.

On October 27, 1983 (48 FR 49808), EPA promulgated portions of the November 26, 1982 proposal, proposed additional changes, and postponed portions of the proposed rule. This final rule included the following:

- Promulgation of BPT TSS limitations for all subcategories equal to a multiple of 1.7 times the existing BPT BOD_5 limitations;

- Promulgation of alternative BPT BOD_5 and COD concentration-based limitations for the extraction, mixing/compounding and formulation, and research subcategories (such alternative limitations

were not deemed necessary for the fermentation and chemical synthesis subcategories because the available data indicated that raw loads were sufficiently high at these subcategory plants that limitations as low as the alternative limitations would not be required under BPT);

- Promulgation of BPT, BAT, NSPS, PSES, and PSNS for cyanide based on monitoring either in-plant after cyanide destruction or end-of-pipe after cyanide destruction and biological treatment for all but the research subcategory;

- Promulgation of pH NSPS for all but the research subcategory;

- Proposal of revised BOD_5 and TSS NSPS based on end-of-pipe filtration in combination with advanced biological treatment for all but the research subcategory;

- Postponement of a final decision on appropriate BAT limitations and NSPS for COD until a later date; and

- Postponement of BCT limitations until promulgation of the general methodology for determining appropriate levels of conventional pollutant control under BCT.

The October 27, 1983 preamble also included a discussion of BAT effluent limitations guidelines, NSPS, PSES, and PSNS for Toxic Volatile Organics (TVOs). The Agency decided, at that time, not to establish regulations controlling the discharge of volatile priority pollutants from pharmaceutical manufacturing plants due to the provisions of Paragraph 8 of the Settlement Agreement, lack of data documenting harmful discharges or POTW pass-through of TVOs, and concern over the costs for treatment. However, the Agency obtained new data regarding the treatment of methylene chloride at a pharmaceutical manufacturing plant during a sampling study in which both the plant and EPA participated and began reconsidering its policy on regulating volatile priority pollutants. On September 9, 1985 (50 FR 36638), the Agency published a Notice of Availability and request for comments for the Pharmaceutical Manufacturing Point Source Category; Effluent Limitations Guidelines, Pretreatment Standards, and New Source Performance Standards (which included the new study data). This notice

requested comments on the treatment of TVOs by steam stripping, pretreatment of wastewaters, and any information about changes in solvent usage and facility flows and treatment operations.

On December 16, 1986 (51 FR 45094), the Agency published a final rule for BCT BOD_5, TSS, and pH effluent limitations guidelines for all but the research subcategory. This final rule set the BCT effluent limitations guidelines equal to the existing BPT BOD_5, TSS, and pH effluent limitations guidelines.

In 1989, EPA withdrew the proposed NSPS for BOD_5 and TSS over Office of Management and Budget (OMB) concern for the cost-effectiveness of TSS control for Subcategories B and D.

1.3 Scope of Proposed Regulations

This proposed regulation covers the fermentation, extraction, chemical synthesis, and mixing, compounding and formulating subcategories of the pharmaceutical manufacturing industry. EPA is proposing to revise the following:

- BPT BOD_5, COD, TSS, and cyanide effluent limitations guidelines;
- BCT BOD_5 and TSS effluent limitations guidelines;
- BAT cyanide effluent limitations guidelines;
- NSPS for BOD_5, TSS, and cyanide; and
- PSES and PSNS for cyanide.

Additionally, EPA is proposing to regulate selected organic constituents, COD, and ammonia under BAT, NSPS, PSES, and PSNS.

These proposed effluent limitations guidelines and standards do not cover discharges generated from the research subcategory of the Pharmaceutical Manufacturing Point Source Category.

1.4 Other Provisions Considered But Not Proposed

EPA is not currently proposing any Best Management Practices (BMPs) for the Pharmaceutical Manufacturing Category. However, EPA is soliciting comment on whether BMPs are applicable to the pharmaceutical industry. A discussion of the Agency's evaluation of potential BMPs for the pharmaceutical industry is presented in Appendix B of this document.

SECTION 2

SUMMARY

2.1 Introduction

The proposed regulations for the pharmaceutical manufacturing industry include effluent limitations guidelines and standards for the control of wastewater pollutants. This document presents the information and rationale supporting these proposed effluent limitations guidelines and standards. Section 2.2 presents the proposed subcategorization scheme, Section 2.3 describes the scope of the proposed regulations, and Section 2.4 through 2.9 summarizes the proposed effluent limitations guidelines and standards.

2.2 Subcategorization

EPA is proposing to maintain the existing subcategorization scheme for this industry (40 CFR Part 439). These subcategories are summarized in the following table:

Subcategory Code (Subpart)	Subcategory
A	Fermentation Operations
B	Biological and Natural Extraction Operations
C	Chemical Synthesis Operations
D	Mixing, Compounding, or Formulating Operations
E	Pharmaceutical Research Operations

2.3 Scope of Proposed Regulations

These proposed regulations apply to Subcategories A through D of the pharmaceutical manufacturing industry. Subcategory E (bench scale pharmaceutical research) operations are not covered by the proposed regulations. Subcategory E operations at stand-alone facilities or at manufacturing facilities with Subcategory A, B, C, and/or D operations will be covered by the existing BPT effluent limitations guidelines for Subcategory E.

Pharmaceutical manufacturers use many different raw materials and manufacturing processes to create a wide range of products with therapeutic value. Pharmaceutical products are produced by chemical synthesis, fermentation, extraction from naturally occurring plant or animal substances, or by refining a technical grade product.

The pharmaceutical products, processes, and activities covered by this proposal include:

- Biological products covered by the 1987 SIC Code 2836 (these products were formerly covered under the 1977 SIC Code 2831) except diagnostic substances.
- Medicinal chemicals and botanical products covered by SIC Code 2833.
- Pharmaceutical products covered by SIC Code 2834.
- All fermentation, biological and natural extraction, chemical synthesis, and formulation products considered as pharmaceutically active ingredients by the Food and Drug Administration that are not covered by SIC Codes 2833, 2834, or 2836.
- Products with multiple end uses which are produced by a pharmaceutical manufacturing operation as a final pharmaceutical product, component of a pharmaceutical formulation, or as a pharmaceutical intermediate. The manufacture of products which have nonpharmaceutical uses is also covered by these proposed regulations provided that the product was primarily intended for use as a pharmaceutical.

- Products not covered by SIC Codes 2833, 2834, and 2836 if they are produced by a pharmaceutical manufacturer by fermentation, biological and natural extraction, chemical synthesis, or mixing, compounding, or formulating operations which generate wastewaters which closely correspond to those of pharmaceutical products.

- Cosmetic preparations covered by SIC Code 2844 which function as a skin treatment. (This group of preparations does not include products such as lipsticks or perfumes which serve to enhance appearance or to provide a pleasing odor, but do not provide skin care. In general, this excludes deodorants, manicure preparations, shaving preparations, and nonmedicated shampoos which do not primarily function as a skin treatment.)

- Pilot-scale activities conducted at pharmaceutical research facilities, such as biological, microbiological, chemical research, and product development activities. (This does not include farms that breed, raise, and/or hold animals for research at another site. This also does not include ordinary feedlot or farm operations utilizing feed that contains pharmaceutically active ingredients.) Pilot-scale pharmaceutical research and product development operations would be subject to the specific manufacturing subcategory limitations and standards corresponding to the subcategory wastewater that the research facility's wastewater resembles. For example, a pilot chemical synthesis operation that generates wastewater that is similar to wastewater generated by chemical synthesis manufacturing would be subject to the subcategory C limitations and standards.

Products or activities specifically excluded from the pharmaceutical manufacturing category include:

- Surgical and medical instruments and apparatus covered by SIC Code No. 3841.

- Orthopedic, prosthetic, and surgical appliances and supplies covered by SIC Code No. 3842.

- Dental equipment and supplies covered by SIC Code No. 3843.

- Medical laboratories covered by SIC Code No. 8071.

- Dental laboratories covered by SIC Code No. 8072.

- Outpatient care facilities covered by SIC Code No. 8081.
- Health and allied services, not elsewhere classified, covered by SIC Code No. 8091.
- Diagnostic devices not covered by SIC Code No. 3841.
- Animal feeds which include pharmaceutically active ingredients such as vitamins and antibiotics. (The major portion of the product is nonpharmaceutical and the wastewater which results from the manufacture of feed is not characteristic of pharmaceutical manufacturing.)
- Foods and beverages which are fortified with vitamins or other pharmaceutically active ingredients. (The major portion of the product is nonpharmaceutical and the wastewater which results from the manufacture of these products is not characteristic of pharmaceutical manufacturing.)

2.4 Best Practicable Control Technology Currently Available (BPT)

EPA is proposing to revise the BPT effluent limitations guidelines for biochemical oxygen demand (BOD_5), chemical oxygen demand (COD), and total suspended solids (TSS) for Subcategories A, B, C, and D. Table 2-1 presents these proposed limitations, which are based on the application of advanced biological treatment. EPA is proposing to revise the BPT effluent limitations guidelines for cyanide for Subcategories A and C. This proposed revision is also presented in Table 2-1 and is based on the application of hydrogen peroxide oxidation for the treatment of cyanide bearing wastewaters. EPA also is proposing to repeal the BPT effluent limitations guidelines for Subcategories B and D because EPA has determined that cyanide is not used or generated in these subcategory operations. The existing BPT effluent limitations guideline for pH is being maintained for all subcategories.

2.5 Best Conventional Pollutant Control Technology (BCT)

EPA is proposing to revise the BCT effluent limitations guidelines for BOD_5 and TSS for Subcategories A, B, C, and D. The proposed BCT effluent limitations guidelines are equal to the proposed BPT effluent limitations and are presented in Table 2-2.

2.6 Best Available Technology Economically Achievable (BAT)

EPA is proposing to revise the BAT effluent limitations guidelines for Subcategories A, B, C, and D. For Subcategories A and C, EPA is proposing BAT effluent limitations for cyanide at an in-plant monitoring point and limitations for ammonia (aqueous), COD, and 53 priority and nonconventional organic pollutants at an end-of-pipe monitoring point. EPA also is soliciting comments and data on whether limits for the 12 most strippable priority and nonconventional organic pollutants should be applied at an in-plant monitoring point (e.g., following steam stripping and prior to dilution with other process and non-process wastewaters not containing these pollutants in treatable quantities and prior to end-of-pipe biological treatment systems). The limits EPA would propose for this in-plant monitoring point are found in Table 2-8. For Subcategories B and D, EPA is proposing BAT effluent limitations for COD, and 53 priority and nonconventional organic pollutants at an end-of-pipe monitoring point. EPA also is proposing to repeal the current BAT effluent limitations for cyanide for Subcategories B and D. Tables 2-3 and 2-4 present these proposed effluent limitations guidelines, which are based on the following: application of in-plant steam stripping and hydrogen peroxide oxidation followed by end-of-pipe advanced biological treatment for Subcategories A and C, and application of end-of-pipe advanced biological treatment for Subcategories B and D. However, as proposed, the limitations for COD are based only on advanced biological treatment. EPA is soliciting comments and data on the extent to which steam stripping also reduces COD and thus contributes to end-of-pipe performance more stringent than proposed.

The proposed regulation for the pharmaceutical manufacturing industry presents analytical method minimum levels in Section 439.1 (g). These values apply to those limitations and standards set at non-detect (ND). For ease of use, the tables presented in this section present the analytical method minimum level in parentheses for those limitations and standards set at ND.

2.7 New Source Performance Standards (NSPS)

EPA is proposing revised NSPS for priority and nonconventional pollutants for Subcategories A, B, C, and D. For Subcategories A and C, EPA is proposing NSPS for cyanide at an in-plant monitoring point based on hydrogen peroxide oxidation and standards for ammonia (aqueous), and 53 priority and nonconventional organic pollutants at an end-of-pipe monitoring point based on in-plant steam stripping with distillation followed by end-of-pipe advanced biological treatment to a treatment level achieved by the best performing facility. EPA also is soliciting comments and data on whether limits for the 12 most strippable priority and nonconventional organic pollutants should be applied at an in-plant monitoring point (e.g., following steam stripping and prior to dilution with other process and non-process wastewaters not containing these pollutants in treatable quantities and prior to end-of-pipe biological treatment systems). The limits EPA would propose for this in-plant monitoring point are found in Table 2-8. EPA also is proposing standards for COD at an end-of-pipe monitoring point based on end-of-pipe advanced biological treatment to a treatment level achieved by the best performing facility. For Subcategories B and D, EPA is proposing NSPS for 53 priority and nonconventional organic pollutants at an end-of-pipe monitoring point based on in-plant steam stripping with distillation followed by end-of-pipe advanced biological treatment to a treatment level achieved by the best performing facility. However, as proposed, the limitations for COD are based only on advanced biological treatment. EPA is soliciting comments and data on the extent to which steam stripping also reduces COD and thus contributes to end-of-pipe performance more stringent than proposed.

EPA is proposing to revise the NSPS controlling discharges of BOD_5, and TSS for Subcategories A, B, C, and D based on advanced biological treatment to a treatment level achieved by the best performing facility. Proposed NSPS for Subcategories A, B, C, and D are presented in Tables 2-5 and 2-6.

The proposed regulation for the pharmaceutical manufacturing industry presents analytical method minimum levels in Section 439.1 (g). These values apply to those limitations and standards set at non-detect (ND). For ease of use, the tables presented in this section present the analytical method minimum level in parentheses for those limitations and standards set at ND.

2.8 Pretreatment Standards for Existing Sources (PSES)

EPA is proposing to revise PSES for Subcategories A, B, C, and D. For Subcategories A, B, C, and D, EPA is proposing PSES based on in-plant steam stripping for 12 priority and nonconventional organic pollutants at an in-plant monitoring point. For Subcategories A and C, EPA is also proposing PSES for cyanide at an in-plant monitoring location based on hydrogen peroxide oxidation. For ammonia and 33 priority and nonconventional organic pollutants, EPA is proposing two different approaches. Under co-proposal (1), EPA is proposing to establish PSES for those pollutants for Subcategories A and/or C at an end-of-pipe monitoring point prior to discharge to the POTW sewer based on in-plant steam stripping. For subcategories B and D under co-proposal (1), EPA is proposing PSES based on in-plant steam stripping for 33 priority and nonconventional organic pollutants at an end-of-pipe monitoring point prior to discharge to the POTW sewer.

Under co-proposal (2), the Agency is proposing PSES at an end-of-pipe monitoring point for ammonia only, based on in-plant steam stripping. The proposed ammonia PSES would apply only to Subcategories A and C. Co-proposal (2) would not include any

standards for the remaining 33 priority and nonconventional organic pollutants (for any subcategory). PSES are presented in Tables 2-7 through 2-10.

The proposed regulation for the pharmaceutical manufacturing industry presents analytical method minimum levels in Section 439.1 (g). These values apply to those limitations and standards set at non-detect (ND). For ease of use, the tables presented in this section present the analytical method minimum level in parentheses for those limitations and standards set at ND.

2.9 Pretreatment Standards for New Sources (PSNS)

EPA is proposing to revise PSNS for Subcategories A, B, C, and D. For all pollutants except cyanide, the PSNS technology basis for the proposed standards is in-plant steam stripping with distillation. For Subcategories A and C, EPA is also proposing PSNS for cyanide at an in-plant monitoring location based on hydrogen peroxide oxidation. As with the proposed PSES, EPA has developed two proposals for PSNS. Under co-proposal (1), for all subcategories, EPA is proposing PSNS for 27 priority and nonconventional organic pollutants at an in-plant monitoring point and PSNS for 18 priority and nonconventional organic pollutants at an end-of-pipe monitoring point prior to discharge to the POTW sewer. For Subcategories A and C, EPA also is proposing PSNS for ammonia at an end-of-pipe monitoring point prior to discharge to the POTW sewer.

Under co-proposal (2), the Agency is proposing PSNS based on in-plant steam stripping with distillation for 12 priority and nonconventional organic pollutants at an in-plant monitoring point for Subcategories A, B, C, and D. The Agency also is proposing PSNS at an end-of-pipe monitoring point prior to discharge to the POTW sewer for ammonia only, for Subcategories A and C. Co-proposal (2) would not include any standards for the remaining 33 priority and nonconventional organic pollutants (for any subcategory). PSNS are presented in Tables 2-11 through 2-14.

The proposed regulation for the pharmaceutical manufacturing industry presents analytical method minimum levels in Section 439.1 (g). These values apply to those limitations and standards set at non-detect (ND). For ease of use, the tables presented in this section present the analytical method minimum level in parentheses for those limitations and standards set at ND.

Table 2-1

Proposed BPT Effluent Limitations for Subcategories A, B, C, and D

Subcategory	Pollutant or Pollutant Property	Proposed BPT Effluent Limitation for End-of-Pipe Monitoring Points (a)	
		Maximum for any one day (mg/L)	Monthly Average (mg/L)
Fermentation Operations	BOD_5	137	58
	COD	1,100	628
	TSS	318	110
	Cyanide	0.766	0.406
Biological and Natural Extraction Operations	BOD_5	37	11
	COD	145	60
	TSS	80	27
Chemical Synthesis Operations	BOD_5	137	58
	COD	1,100	628
	TSS	318	110
	Cyanide	0.766	0.406
Mixing, Compounding, or Formulating Operations	BOD_5	37	11
	COD	145	60
	TSS	80	27

(a)BPT standards for cyanide apply at an in-plant location (i.e., the treatment location of cyanide-bearing wastestreams).

Table 2-2

Proposed BCT Effluent Limitations for Subcategories A, B, C, and D

Subcategory	Pollutant or Pollutant Property	Proposed BCT Effluent Limitation for End-of-Pipe Monitoring Points	
		Maximum for any one day (mg/L)	Monthly Average (mg/L)
Fermentation Operations	BOD_5 TSS	137 318	58 110
Biological and Natural Extraction Operations	BOD_5 TSS	37 80	11 27
Chemical Synthesis Operations	BOD_5 TSS	137 318	58 110
Mixing, Compounding, or Formulating Operations	BOD_5 TSS	37 80	11 27

Table 2-3

Proposed BAT Effluent Limitations for Subcategory A - Fermentation Operations and Subcategory C - Chemical Synthesis Operations

Pollutant or Pollutant Property	Proposed BAT Effluent Limitations for In-Plant Monitoring Points	
	Maximum for any 1 day µg/L	Monthly Average µg/L
Cyanide	766	406

Pollutant or Pollutant Property	Proposed BAT Effluent Limitations for End-of-Pipe Monitoring Points	
	Maximum for any 1 day µg/L	Monthly Average µg/L
Acetone	ND (50)	ND (50)
Acetonitrile	ND (5,000)	ND (5,000)
Ammonia	4,850	3,230
n-Amyl Acetate	105	45
Amyl Alcohol	668	ND (500)
Aniline	10	10
Benzene	ND (10)	ND (10)
2-Butanone (MEK)	202	86
n-Butyl Acetate	87	37
n-Butyl Alcohol	ND (500)	ND (500)
tert-Butyl Alcohol	668	284
Chemical Oxygen Demand (COD)	1,100,000	628,000
Chlorobenzene	ND (10)	ND (10)
Chloroform	ND (10)	ND (10)
Chloromethane	ND (50)	ND (50)
Cyclohexane	ND(5)	ND(5)
o-Dichlorobenzene	ND (10)	ND (10)
1,2-Dichloroethane	100	35

Table 2-3

(Continued)

Pollutant or Pollutant Property	Proposed BAT Effluent Limitations for End-of-Pipe Monitoring Points	
	Maximum for any 1 day µg/L	Monthly Average µg/L
Diethylamine	ND (50,000)	ND (50,000)
Diethyl Ether	574	244
Dimethylamine	ND (50,000)	ND (50,000)
N,N-Dimethylacetamide	ND (50)	ND (50)
N,N-Dimethylaniline	50	50
N,N-Dimethylformamide	45	19
Dimethyl Sulfoxide	ND (20,000)	ND (20,000)
1,4-Dioxane	220	94
Ethanol	ND (3,180)	ND (3,180)
Ethyl Acetate	105	45
Ethylene Glycol	ND (100,000)	ND (100,000)
Formaldehyde	1,480	623
Formamide	ND (100,000)	ND (100,000)
Furfural	2,670	1,140
n-Heptane	ND (10)	ND (10)
n-Hexane	ND (10)	ND (10)
Isobutyraldehyde	1,370	581
Isopropanol	ND (200)	ND (200)
Isopropyl Acetate	87	37
Isopropyl Ether	574	244
Methanol	ND (3,180)	ND (3,180)
Methylamine	ND (50,000)	ND (50,000)
Methyl Cellosolve	ND (20,000)	ND (20,000)
Methyl Formate	105	ND (100)

Table 2-3

(Continued)

Pollutant or Pollutant Property	Proposed BAT Effluent Limitations for End-of-Pipe Monitoring Points	
	Maximum for any 1 day µg/L	Monthly Average µg/L
Methylene Chloride	ND (10)	ND (10)
MIBK	ND (10)	ND (10)
2-Methylpyridine	50	50
Petroleum Naphtha	ND (10)	ND (10)
Phenol	25	14
Polyethylene Glycol 600	4,870	2,070
n-Propanol	ND (3,180)	ND (3,180)
Pyridine	10	10
Tetrahydrofuran	910	264
Toluene	ND (10)	ND (10)
Trichlorofluoromethane	ND (10)	ND (10)
Triethylamine	ND (50,000)	ND (50,000)
Xylenes	ND (10)	ND (10)

ND - Nondetect - A concentration-based measurement reported below the minimum level that can be reliably measured by the analytical method for the pollutant. Minimum levels are presented in parentheses corresponding to an analytical method applicable to the respective pollutant.

Table 2-4

Proposed BAT Effluent Limitations for Subcategory B - Biological and Natural Extraction Operations and Subcategory D - Mixing, Compounding, or Formulating Operations

Pollutant or Pollutant Property	Proposed BAT Effluent Limitations for End-of-Pipe Monitoring Points	
	Maximum for any 1 day µg/L	Monthly Average µg/L
Acetone	413	178
Acetonitrile	ND (5,000)	ND (5,000)
n-Amyl Acetate	3,000	1,280
Amyl Alcohol	3,980	1,690
Aniline	10	10
Benzene	40	17
2-Butanone (MEK)	202	86
n-Butyl Acetate	500	500
n-Butyl Alcohol	ND (500)	ND (500)
tert-Butyl Alcohol	3,980	1,690
Chemical Oxygen Demand (COD)	145,000	59,900
Chlorobenzene	ND (10)	ND (10)
Chloroform	22	13
Chloromethane	206	87
Cyclohexane	ND (5)	ND (5)
o-Dichlorobenzene	ND (10)	ND (10)
1,2-Dichloroethane	438	152
Diethylamine	ND (50,000)	ND (50,000)
Diethyl Ether	4,870	2,070
N,N-Dimethylacetamide	ND (50)	ND (50)
Dimethylamine	ND (50,000)	ND (50,000)
N,N-Dimethylaniline	50	50
N,N-Dimethylformamide	45	19
Dimethyl Sulfoxide	ND (20,000)	ND (20,000)
1,4-Dioxane	220	94
Ethanol	ND (3,180)	ND (3,180)
Ethyl Acetate	3,000	1,280
Ethylene Glycol	ND (100,000)	ND (100,000)

Table 2-4

(Continued)

Pollutant or Pollutant Property	Proposed BAT Effluent Limitations for End-of-Pipe Monitoring Points	
	Maximum for any 1 day µg/L	Monthly Average µg/L
Formaldehyde	1,480	623
Formamide	ND (100,000)	ND (100,000)
Furfural	3,000	1,280
n-Heptane	ND (10)	ND (10)
n-Hexane	ND (10)	ND (10)
Isobutyraldehyde	1,370	581
Isopropanol	1,120	476
Isopropyl Acetate	500	500
Isopropyl Ether	4,870	2,070
Methanol	6,660	ND (3,180)
Methylamine	ND (50,000)	ND (50,000)
Methyl Cellosolve	ND (20,000)	ND (20,000)
Methylene Chloride	1,420	357
Methyl Formate	3,000	1,280
MIBK	119	51
2-Methylpyridine	50	50
Petroleum Naphtha	40	17
Phenol	25	14
Polyethylene Glycol 600	4,870	2,070
n-Propanol	3,980	ND (3,180)
Pyridine	10	10
Tetrahydrofuran	15,000	4,350
Toluene	40	17
Trichlorofluoromethane	599	322
Triethylamine	ND (50,000)	ND (50,000)
Xylenes	ND (10)	ND (10)

ND - Nondetect - A concentration-based measurement reported below the minimum level that can be reliably measured by the analytical method for the pollutant. Minimum levels are presented in parentheses corresponding to an analytical method applicable to the respective pollutant.

Table 2-5

Proposed NSPS for Subcategory A - Fermentation Operations and Subcategory C - Chemical Synthesis Operations

Pollutant or Pollutant Property	Proposed NSPS for In-Plant Monitoring Points	
	Maximum for any 1 day µg/L	Monthly Average µg/L
Cyanide	766	406

Pollutant or Pollutant Property	Proposed NSPS for End-of-Pipe Monitoring Points	
	Maximum for any 1 day µg/L	Monthly Average µg/L
Acetone	ND (50)	ND (50)
Acetonitrile	ND (5,000)	ND (5,000)
Ammonia	4,850	3,230
n-Amyl Acetate	14	6
Amyl Alcohol	ND (500)	ND (500)
Aniline	10	4
Benzene	ND (10)	ND (10)
2-Butanone (MEK)	144	61
n-Butyl Acetate	11	ND (5)
n-Butyl Alcohol	ND (500)	ND (500)
tert-Butyl Alcohol	ND (100)	ND (100)
Chlorobenzene	ND (10)	ND (10)
Chloroform	ND (10)	ND (10)
Chloromethane	ND (50)	ND (50)
Cyclohexane	ND (5)	ND (5)
o-Dichlorobenzene	ND (10)	ND (10)
1,2-Dichloroethane	13	ND (10)
Diethylamine	ND (50,000)	ND (50,000)
Diethyl Ether	74	ND (50)
N,N-Dimethylacetamide	ND (50)	ND (50)
Dimethylamine	ND (50,000)	ND (50,000)
N,N-Dimethylaniline	50	45
N,N-Dimethylformamide	45	19
Dimethyl Sulfoxide	ND (20,000)	ND (20,000)
1,4-Dioxane	ND (50)	ND (50)
Ethanol	ND (3,180)	ND (3,180)
Ethyl Acetate	14	ND (10)

Table 2-5

(Continued)

Pollutant or Pollutant Property	Proposed NSPS for End-of-Pipe Monitoring Points	
	Maximum for any 1 day µg/L	Monthly Average µg/L
Ethylene Glycol	ND (100,000)	ND (100,000)
Formaldehyde	1,480	623
Formamide	ND (100,000)	ND (100,000)
Furfural	53	ND (50)
n-Heptane	ND (10)	ND (10)
n-Hexane	ND (10)	ND (10)
Isobutyraldehyde	304	129
Isopropanol	ND (200)	ND (200)
Isopropyl Acetate	11	ND (10)
Isopropyl Ether	74	32
MIBK	ND (10)	ND (10)
Methanol	ND (3,180)	ND (3,180)
Methylamine	ND (50,000)	ND (50,000)
Methyl Cellosolve	ND (20,000)	ND (20,000)
Methylene Chloride	ND (10)	ND (10)
Methyl Formate	ND (100)	ND (100)
2-Methylpyridine	50	45
Petroleum Naphtha	ND (10)	ND (10)
Phenol	25	14
Polyethylene Glycol 600	4,870	2,070
n-Propanol	ND (3,180)	ND (3,180)
Pyridine	10	10
Tetrahydrofuran	910	264
Toluene	ND (10)	ND (10)
Trichlorofluoromethane	ND (10)	ND (10)
Triethylamine	ND (50,000)	ND (50,000)
Xylenes	ND (10)	ND (10)
BOD_5 (mg/L)	62	29
COD (mg/L)	781	538
TSS (mg/L)	87	43

ND - Nondetect - A concentration-based measurement reported below the minimum level that can be reliably measured by the analytical method for the pollutant. Minimum levels are presented in parentheses corresponding to an analytical method applicable to the respective pollutant.

Table 2-6

Proposed NSPS for Subcategory B - Biological and Natural Extraction Operations and Subcategory D - Mixing, Compounding, or Formulating Operations

Pollutant or Pollutant Property	Proposed NSPS for End-of-Pipe Monitoring Points	
	Maximum for any 1 day µg/L	Monthly Average µg/L
Acetone	ND (50)	ND (50)
Acetonitrile	ND (5,000)	ND (5,000)
n-Amyl Acetate	14	6
Amyl Alcohol	ND (500)	ND (500)
Aniline	10	4
Benzene	ND (10)	ND (10)
2-Butanone (MEK)	144	61
n-Butyl Acetate	11	ND (5)
n-Butyl Alcohol	ND (500)	ND (500)
tert-Butyl Alcohol	ND (100)	ND (100)
Chlorobenzene	ND (10)	ND (10)
Chloroform	ND (10)	ND (10)
Chloromethane	ND (50)	ND (50)
Cyclohexane	ND (5)	ND (5)
o-Dichlorobenzene	ND (10)	ND (10)
1,2-Dichloroethane	13	ND (10)
Diethylamine	ND (50,000)	ND (50,000)
Diethyl Ether	74	ND (50)
N,N-Dimethylacetamide	ND (50)	ND (50)
N,N-Dimethylaniline	50	45
N,N-Dimethylformamide	45	19
Dimethylamine	ND (50,000)	ND (50,000)
Dimethyl Sulfoxide	ND (20,000)	ND (20,000)
1,4-Dioxane	ND (50)	ND (50)
Ethanol	ND (3,180)	ND (3,180)
Ethyl Acetate	14	ND (10)
Ethylene Glycol	ND (100,000)	ND (100,000)
Formaldehyde	1,480	623
Formamide	ND (100,000)	ND (100,000)
Furfural	53	ND (50)
n-Heptane	ND (10)	ND (10)
n-Hexane	ND (10)	ND (10)

Table 2-6

(Continued)

Pollutant or Pollutant Property	Proposed NSPS for End-of-Pipe Monitoring Points	
	Maximum for any 1 day µg/L	Monthly Average µg/L
Isobutyraldehyde	304	129
Isopropanol	ND (200)	ND (200)
Isopropyl Acetate	11	ND (10)
Isopropyl Ether	74	32
MIBK	ND (10)	ND (10)
Methanol	ND (3,180)	ND (3,180)
Methylamine	ND (50,000)	ND (50,000)
Methyl Cellosolve	ND (20,000)	ND (20,000)
Methyl Formate	ND (100)	ND (100)
Methylene Chloride	ND (10)	ND (10)
2-Methylpyridine	50	45
Petroleum Naphtha	ND (10)	ND (10)
Phenol	25	14
Polyethylene Glycol 600	4,870	2,070
n-Propanol	ND (3,180)	ND (3,180)
Pyridine	10	10
Tetrahydrofuran	910	264
Toluene	ND (10)	ND (10)
Trichlorofluoromethane	ND (10)	ND (10)
Triethylamine	ND (50,000)	ND (50,000)
Xylenes	ND (10)	ND (10)
BOD_5 (mg/L)	34	10
COD (mg/L)	60	24
TSS (mg/L)	40	12

ND - Nondetect - A concentration-based measurement reported below the minimum level that can be reliably measured by the analytical method for the pollutant. Minimum levels are presented in parentheses corresponding to an analytical method applicable to the respective pollutant.

Table 2-7

Proposed PSES for Subcategory A - Fermentation Operations and Subcategory C - Chemical Synthesis Operations - Co-Proposal (1)

Pollutant or Pollutant Property	Proposed PSES for In-Plant Monitoring Points	
	Maximum for any 1 day µg/L	Monthly Average µg/L
Benzene	796	268
Chlorobenzene	796	268
Chloroform	ND (10)	ND (10)
Chloromethane	796	268
Cyanide	766	406
Cyclohexane	796	268
n-Heptane	796	268
n-Hexane	796	268
Methyl Cellosolve	ND (20,000)	ND (20,000)
Methylene Chloride	809	279
Toluene	198	148
Trichlorofluoromethane	796	268
Xylenes	796	268

Pollutant or Pollutant Property	Proposed PSES for End-of-Pipe Monitoring Points	
	Maximum for any 1 day µg/L	Monthly Average µg/L
Acetone	31,400	9,690
Ammonia	12,900	10,900
n-Amyl Acetate	23,900	8,050
Amyl Alcohol	607,000	205,000
Aniline	10,900,000	3,690,000
2-Butanone (MEK)	1,440,000	430,000
n-Butyl Acetate	23,900	8,050
n-Butyl Alcohol	10,900,000	3,690,000
tert-Butyl Alcohol	607,000	205,000
o-Dichlorobenzene	23,900	8,050
1,2-Dichloroethane	23,900	8,050
Diethylamine	ND (50,000)	ND (50,000)

Table 2-7

(Continued)

Pollutant or Pollutant Property	Proposed PSES for End-of-Pipe Monitoring Points	
	Maximum for any 1 day µg/L	Monthly Average µg/L
Diethyl Ether	23,900	8,050
Dimethylamine	607,000	205,000
N,N-Dimethylaniline	607,000	205,000
1,4-Dioxane	10,900,000	3,690,000
Ethanol	2,200,000	784,000
Ethyl Acetate	23,900	8,050
Formamide	607,000	205,000
Furfural	607,000	205,000
Isobutyraldehyde	23,900	8,050
Isopropanol	597,000	198,000
Isopropyl Acetate	23,900	8,050
Isopropyl Ether	23,900	8,050
Methanol	11,700,000	3,800,000
Methylamine	607,000	205,000
Methyl Formate	23,900	8,050
MIBK	23,900	8,050
2-Methylpyridine	607,000	205,000
Petroleum Naphtha	10,900,000	3,690,000
n-Propanol	2,790,000	941,000
Pyridine	1,000	1,000
Tetrahydrofuran	9,210	3,360
Triethylamine	ND (50,000)	ND (50,000)

ND - Nondetect - A concentration-based measurement reported below the minimum level that can be reliably measured by the analytical method for the pollutant. Minimum levels are presented in parentheses corresponding to an analytical method applicable to the respective pollutant.

Table 2-8

Proposed PSES for Subcategory A - Fermentation Operations and Subcategory C - Chemical Synthesis Operations - Co-Proposal (2)

Pollutant or Pollutant Property	Proposed PSES for In-Plant Monitoring Points	
	Maximum for any 1 day µg/L	Monthly Average µg/L
Benzene	796	268
Chlorobenzene	796	268
Chloroform	ND (10)	ND (10)
Chloromethane	796	268
Cyanide	766	406
Cyclohexane	796	268
n-Heptane	796	268
n-Hexane	796	268
Methyl Cellosolve	ND (20,000)	ND (20,000)
Methylene Chloride	809	279
Toluene	198	148
Trichlorofluoromethane	796	268
Xylenes	796	268

Pollutant or Pollutant Property	Proposed PSES for End-of-Pipe Monitoring Points	
	Maximum for and 1 day µg/L	Monthly Average µg/L
Ammonia	12,900	10,900

ND - Nondetect - A concentration-based measurement reported below the minimum level that can be reliably measured by the analytical method for the pollutant. Minimum levels are presented in parentheses corresponding to an analytical method applicable to the respective pollutant.

Table 2-9

Proposed PSES for Subcategory B - Biological and Natural Extraction Operations and Subcategory D - Mixing, Compounding, or Formulating - Co-Proposal(1)

Pollutant or Pollutant Property	Proposed PSES for In-Plant Monitoring Points	
	Maximum for any 1 day µg/L	Monthly Average µg/L
Benzene	796	268
Chlorobenzene	796	268
Chloroform	ND (10)	ND (10)
Chloromethane	796	268
Cyclohexane	796	268
n-Heptane	796	268
n-Hexane	796	268
Methyl Cellosolve	ND (20,000)	ND (20,000)
Methylene Chloride	809	279
Toluene	198	148
Trichlorofluoromethane	796	268
Xylenes	796	268

Pollutant or Pollutant Property	Proposed PSES for End-of-Pipe Monitoring Points	
	Maximum for any 1 day µg/L	Monthly Average µg/L
Acetone	31,400	9,690
n-Amyl Acetate	23,900	8,050
Amyl Alcohol	607,000	205,000
Aniline	10,900,000	3,690,000
2-Butanone (MEK)	1,440,000	430,000
n-Butyl Acetate	23,900	8,050
n-Butyl Alcohol	10,900,000	3,690,000
tert-Butyl Alcohol	607,000	205,000
o-Dichlorobenzene	23,900	8,050
1,2-Dichloroethane	23,900	8,050
Diethylamine	ND (50,000)	ND (50,000)
Diethyl Ether	23,900	8,050

Table 2-9

(Continued)

Pollutant or Pollutant Property	Proposed PSES for End-of-Pipe Monitoring Points	
	Maximum for any 1 day µg/L	Monthly Average µg/L
Dimethylamine	607,000	205,000
N,N-Dimethylaniline	607,000	205,000
1,4-Dioxane	10,900,000	3,690,000
Ethanol	2,200,000	784,000
Ethyl Acetate	23,900	8,050
Formamide	607,000	205,000
Furfural	607,000	205,000
Isobutyraldehyde	23,900	8,050
Isopropanol	597,000	198,000
Isopropyl Acetate	23,900	8,050
Isopropyl Ether	23,900	8,050
Methanol	11,700,000	3,800,000
Methylamine	607,000	205,000
Methyl Formate	23,900	8,050
MIBK	23,900	8,050
2-Methylpyridine	607,000	205,000
Petroleum Naphtha	10,900,000	3,690,000
n-Propanol	2,790,000	941,000
Pyridine	1,000	1,000
Tetrahydrofuran	9,210	3,360
Triethylamine	ND (50,000)	ND (50,000)

ND - Nondetect - A concentration-based measurement reported below the minimum level that can be reliably measured by the analytical method for the pollutant. Minimum levels are presented in parentheses corresponding to an analytical method applicable to the respective pollutant.

Table 2-10

Proposed PSES for Subcategory B - Biological and Natural Extraction Operations and Subcategory D - Mixing, Compounding, or Formulating Operations - Co-Proposal (2)

Pollutant or Pollutant Property	Proposed PSES for In-Plant Monitoring Points	
	Maximum for any 1 day µg/L	Monthly Average µg/L
Benzene	796	268
Chlorobenzene	796	268
Chloroform	ND (10)	ND (10)
Chloromethane	796	268
Cyclohexane	796	268
n-Heptane	796	268
n-Hexane	796	268
Methyl Cellosolve	ND (20,000)	ND (20,000)
Methylene Chloride	809	279
Toluene	198	148
Trichlorofluoromethane	796	268
Xylenes	796	268

ND - Nondetect - A concentration-based measurement reported below the minimum level that can be reliably measured by the analytical method for the pollutant. Minimum levels are presented in parentheses corresponding to an analytical method applicable to the respective pollutant.

Table 2-11

Proposed PSNS for Subcategory A - Fermentation Operations and Subcategory C - Chemical Synthesis Operations - Co-Proposal (1)

Pollutant or Pollutant Property	Proposed PSNS for In-Plant Monitoring Points	
	Maximum for any 1 day µg/L	Monthly Average µg/L
Acetone	1,190	600
Amyl Alcohol	8,690	3,220
Benzene	573	212
n-Butyl Alcohol	8,690	3,220
tert-Butyl Alcohol	8,690	3,220
Chlorobenzene	573	212
Chloroform	ND (10)	ND (10)
Chloromethane	573	212
Cyanide	766	406
Cyclohexane	573	212
Diethylamine	ND (50,000)	ND (50,000)
Diethyl Ether	2,230	826
Dimethylamine	ND (50,000)	ND (50,000)
Ethanol	8,690	3,220
Formamide	ND (100,000)	ND (100,000)
n-Heptane	573	212
n-Hexane	573	212
Isopropanol	8,690	3,220
Methanol	8,320	ND (3,180)
Methylamine	ND (50,000)	ND (50,000)
Methyl Cellosolve	ND (20,000)	ND (20,000)
Methylene Chloride	809	279
Methyl Formate	2,230	826
n-Propanol	8,690	3,220
Toluene	184	135
Trichlorofluoromethane	573	212
Triethylamine	ND (50,000)	ND (50,000)
Xylenes	573	212

Table 2-11

(Continued)

Pollutant or Pollutant Property	Proposed PSNS for End-of-Pipe Monitoring Points	
	Maximum for any 1 day µg/L	Monthly Average µg/L
Ammonia	12,900	10,900
n-Amyl Acetate	2,230	826
Aniline	8,690	3,220
2-Butanone (MEK)	161,000	57,900
n-Butyl Acetate	2,230	826
o-Dichlorobenzene	2,230	826
1,2-Dichloroethane	2,230	826
N,N-Dimethylaniline	8,690	3,220
1,4-Dioxane	8,690	3,220
Ethyl Acetate	2,230	826
Furfural	8,690	3,220
Isobutyraldehyde	2,230	826
Isopropyl Acetate	2,230	826
Isopropyl Ether	2,230	826
MIBK	2,230	826
2-Methylpyridine	8,690	3,220
Petroleum Naphtha	8,690	3,220
Pyridine	1,000	1,000
Tetrahydrofuran	9,210	3,360

ND - Nondetect - A concentration-based measurement reported below the minimum level that can be reliably measured by the analytical method for the pollutant. Minimum levels are presented in parentheses corresponding to an analytical method applicable to the respective pollutant.

Table 2-12

Proposed PSNS for Subcategory A - Fermentation Operations and Subcategory C - Chemical Synthesis Operations - Co-Proposal (2)

Pollutant or Pollutant Property	Proposed PSNS for In-Plant Monitoring Points	
	Maximum for any 1 day µg/L	Monthly Average µg/L
Benzene	573	212
Chlorobenzene	573	212
Chloroform	ND (10)	ND (10)
Chloromethane	573	212
Cyanide	766	406
Cyclohexane	573	212
n-Heptane	573	212
n-Hexane	573	212
Methyl Cellosolve	ND (20,000)	ND (20,000)
Methylene Chloride	809	279
Toluene	184	135
Trichlorofluoromethane	573	212
Xylenes	573	212

Pollutant or Pollutant Property	Proposed PSNS for End-of-Pipe Monitoring Points	
	Maximum for any 1 day µg/L	Monthly Average µg/L
Ammonia	12,900	10,900

ND - Nondetect - A concentration-based measurement reported below the minimum level that can be reliably measured by the analytical method for the pollutant. Minimum levels are presented in parentheses corresponding to an analytical method applicable to the respective pollutant.

Table 2-13

Proposed PSNS for Subcategory B - Biological and Natural Extraction Operations and Subcategory D - Mixing, Compounding, or Formulating Operations - Co-Proposal (1)

Pollutant or Pollutant Property	Proposed PSNS for In-Plant Monitoring Points	
	Maximum for any 1 day µg/L	Monthly Average µg/L
Acetone	1,190	600
Amyl Alcohol	8,690	3,220
Benzene	573	212
n-Butyl Alcohol	8,690	3,220
tert-Butyl Alcohol	8,690	3,220
Chlorobenzene	573	212
Chloroform	ND (10)	ND (10)
Chloromethane	573	212
Cyclohexane	573	212
Diethylamine	ND (50,000)	ND (50,000)
Diethyl Ether	2,230	826
Dimethylamine	ND (50,000)	ND (50,000)
Ethanol	8,690	3,220
Formamide	ND (100,000)	ND (100,000)
n-Heptane	573	212
n-Hexane	573	212
Isopropanol	8,690	3,220
Methanol	8,320	ND (3,180)
Methylamine	ND (50,000)	ND (50,000)
Methyl Cellosolve	ND (20,000)	ND (20,000)
Methylene Chloride	809	279
Methyl Formate	2,230	826
n-Propanol	8,690	3,220
Toluene	184	135
Trichlorofluoromethane	573	212
Triethylamine	ND (50,000)	ND (50,000)
Xylenes	573	212

Table 2-13

(Continued)

Pollutant or Pollutant Property	Proposed PSNS for End-of-Pipe Monitoring Points	
	Maximum for any 1 day µg/L	Monthly Average µg/L
n-Amyl Acetate	2,230	826
Aniline	8,690	3,220
2-Butanone (MEK)	161,000	57,900
n-Butyl Acetate	2,230	826
o-Dichlorobenzene	2,230	826
1,2-Dichloroethane	2,230	826
N,N-Dimethylaniline	8,690	3,220
1,4-Dioxane	8,690	3,220
Ethyl Acetate	2,230	826
Furfural	8,690	3,220
Isobutyraldehyde	2,230	826
Isopropyl Acetate	2,230	826
Isopropyl Ether	2,230	826
MIBK	2,230	826
2-Methylpyridine	8,690	3,220
Petroleum Naphtha	8,690	3,220
Pyridine	1,000	1,000
Tetrahydrofuran	9,210	3,360

ND - Nondetect - A concentration-based measurement reported below the minimum level that can be reliably measured by the analytical method for the pollutant. Minimum levels are presented in parentheses corresponding to an analytical method applicable to the respective pollutant.

Table 2-14

Proposed PSNS for Subcategory B - Biological and Natural Extraction Operations and Subcategory D - Mixing, Compounding, or Formulating Operations - Co-Proposal (2)

Pollutant or Pollutant Property	Proposed PSNS for In-Plant Monitoring Points	
	Maximum for any 1 day µg/L	Monthly Average µg/L
Benzene	573	212
Chlorobenzene	573	212
Chloroform	ND (10)	ND (10)
Chloromethane	573	212
Cyclohexane	573	212
n-Heptane	573	212
n-Hexane	573	212
Methyl Cellosolve	ND (20,000)	ND (20,000)
Methylene Chloride	809	279
Toluene	184	135
Trichlorofluoromethane	573	212
Xylenes	573	212

ND - Nondetect - A concentration-based measurement reported below the minimum level that can be reliably measured by the analytical method for the pollutant. Minimum levels are presented in parentheses corresponding to an analytical method applicable to the respective pollutant.

SECTION 3

INDUSTRY DESCRIPTION

3.1 Introduction

This section describes the pharmaceutical manufacturing industry by presenting a summary of the data and information EPA has gathered from previous EPA rulemaking efforts along with data collected as part of this effort to develop revised effluent limitations guidelines and standards for the pharmaceutical manufacturing industry. The following topics are discussed in this section:

- Section 3.2 discusses EPA's data collection methods and information sources;
- Section 3.3 presents an overview of the industry;
- Section 3.4 discusses pharmaceutical manufacturing processes; and
- Section 3.5 discusses trends in the industry.

3.2 Data Collection Methodology and Information Sources

In the course of developing effluent limitations guidelines and standards for the pharmaceutical manufacturing industry, EPA gathered and evaluated technical data from various sources to create an industry profile with respect to manufacturing processes, geographical distribution of facilities, and wastewater generation, treatment, and disposal. These data have also been used to characterize the pharmaceutical manufacturing industry's wastewater by evaluating the industry's water use, type of wastewater discharge, and occurrence of conventional, priority, and nonconventional pollutants in the wastewater. This section summarizes the data collection efforts undertaken by EPA from 1975 to the present.

EPA announced it would collect additional information on this industry by publishing a Federal Register Notice (50 FR 36638, September 9, 1985) indicating its intent to reconsider whether or not to regulate methylene chloride and other volatile priority pollutants. In that Notice, EPA declared it had received new information indicating methylene chloride causes cancer in animals, such that the effects of methylene chloride discharges from pharmaceutical manufacturing plants may be more harmful than previously believed. Additionally, the results of the 1986 Domestic Sewage Study (DSS) (1) identified pharmaceutical manufacturing facilities as a significant source of organic pollutants, and found that discharges of organic compounds from these facilities are largely unregulated. Based on these data, EPA ranked this industry relatively high with respect to other industries in EPA's Section 304(m) plan due to environmental need (volatile organic discharges) and utility to permits and pretreatment programs. Because of the DSS findings, EPA decided to expand its review beyond priority pollutants to include this industry's use and disposition of approximately 250 additional nonconventional pollutants.

Before introducing extensive new data collection efforts, EPA reviewed in 1986 available information and identified missing information that would need to be obtained for the review and revision of current effluent limitations guidelines and standards for this industry. Section 3.2.1 summarizes the data and information already available to EPA prior to 1986. Sections 3.2.2 through 3.2.9 describe EPA's new data collection efforts.

3.2.1 Summary of Data Collection Efforts

Data collection efforts conducted by EPA prior to 1986 provided substantial information regarding manufacturing processes, water use, wastewater characteristics, and treatment technologies in the pharmaceutical manufacturing industry. Documentation of these efforts was reviewed in 1986 to identify data and information that would be useful to the effort to develop revised effluent limitations guidelines and standards for the

pharmaceutical manufacturing industry. This review identified the following major sources of information:

- 308 Portfolio Survey. The original 308 Portfolio Survey was an invaluable source of information for developing an industry profile and characterizing industry wastes. It provided the first detailed information on conventional pollutant parameters in the industry's wastewater and wastewater flow characteristics. It was also the first major data source on the use and/or generation of priority pollutants by this industry.

  The 308 Portfolio Survey was conducted in two phases. In the fall of 1977, EPA distributed the original questionnaire to members of the Pharmaceutical Manufacturers' Association (PMA). (Now the Pharmaceutical Research and Manufacturers Association, PhRMA.) The Agency then distributed a second questionnaire to the remainder of the industry in the spring of 1979.

- PEDCo Reports. In the late 1970s, and concurrent with the data-gathering efforts of the 308 Portfolio Survey, PEDCo Environmental, Inc. (PEDCo), reviewed available literature to identify priority pollutants associated with the production of various pharmaceutical products.(2)(3)(4)

- OAQPS Study. EPA's Office of Air Quality Planning and Standards (OAQPS), with the assistance of the PMA, conducted a survey to determine the use and disposition of the 10 largest volume volatile organic pollutants that each member company purchased in 1975.(5)

  In 1985, OAQPS, with the assistance of the PMA, obtained updated purchase and disposition data for selected solvents from PMA member companies.(6) These data were added to the same type of industry data collected by OAQPS in 1975; both data sets are discussed in more detail in Section 5.

- Screening and Verification Sampling Program. Beginning in 1978, EPA initiated the Screening and Verification Sampling Program, under which wastewater samples were collected from plants with manufacturing operations representative of the industry. Process and end-of-pipe wastewater samples were collected and analyzed for priority, conventional, and nonconventional pollutants in a two-phase program. The first phase, called the screening phase,

involved sampling and analyzing the effluent from 26 plants to determine the presence of conventional, priority, and nonconventional pollutants. This phase was followed by a verification phase, in which multiple samples were collected over several days at five facilities to verify the presence of the pollutants detected during the screening phase. Data from the Screening and Verification Sampling Program, augmented by data collected more recently, were used by EPA to characterize pharmaceutical industry wastewater.

- RSKERL/ADA Study. In 1979, the Robert S. Kerr Environmental Research Laboratory at Ada, Oklahoma (RSKERL/ADA) conducted an applied research study entitled "Industry Fate Study."(7) The purpose of this report was to determine the fate of specific priority pollutants within a biological treatment system. During the study, priority pollutants associated with the manufacture of pharmaceuticals were identified at two industrial facilities.

- Toxic Volatile Organics (TVO) Questionnaire. In 1982, EPA distributed a survey to 15 pharmaceutical manufacturing facilities requesting analytical information on TVO levels in their process wastewater. The survey was limited to volatile organic priority pollutants only.

- Steam Stripper Sampling. In May of 1983, EPA collected influent and effluent wastewater samples from a packed column steam stripper and a steam distillation flash tank at Plant 12003. The study was conducted over a five-day period, and provided EPA with analytical data documenting the performance of this technology treating pharmaceutical manufacturing industry wastewaters.

- Pilot-Plant Carbon Study. In 1984, U.S. EPA's Water Engineering Research Laboratory (WERL) conducted a pilot-plant carbon study to determine constituents contributing to high chemical oxygen demand (COD) in pharmaceutical manufacturing industry effluents, and to evaluate the ability of activated carbon adsorption technology to reduce COD levels.

- Domestic Sewage Study. In 1985, EPA sampled a pharmaceutical manufacturing facility as part of its efforts to evaluate the discharge of priority and hazardous pollutants to POTWs.(1) Samples of the raw wastewater discharge to the local POTW were taken at Plant 30767 during a 24-hour period.

Data from the above sources were evaluated and summarized in 1986. Additional data collection efforts were then undertaken to fill the data gaps identified during the analysis of the above data and to update or replace outdated information. The new data collection efforts were:

- A follow-up (to the 1984 WERL study) pilot plant carbon study in 1987;
- Sampling and analysis of wastewater at 13 pharmaceutical manufacturing facilities between 1986 and 1991;
- A screener questionnaire distributed in May 1989 and a detailed questionnaire distributed in September 1991;
- Industry self-monitoring data submitted to EPA with the Detailed Questionnaire;
- EPA bench- and pilot-scale steam stripping, air stripping, and distillation treatability studies in 1991 and 1993.
- Product patent reviews for solvent usage;
- POTW Survey distributed in 1993 to nine POTWs receiving wastewater from pharmaceutical manufacturers; and
- Annual pollutant disposition data submitted by industry for the years 1987 through 1990 as part of their requirements under Section 313 of the Emergency Planning and Community Right to Know Act of 1986 [Toxic Release Inventory (TRI) data].

Detailed discussions of these data collection efforts are presented in Sections 3.2.2 through 3.2.9.

3.2.2 Follow-up Pilot-Plant Carbon Study

EPA conducted a follow-up pilot-plant powdered activated carbon (PAC) study in 1987. The purpose of the study was to reduce COD concentrations by using PAC in

pharmaceutical manufacturing wastewater biological treatment systems without creating additional mixed liquor suspended solids in the wastewater.

3.2.3 EPA's 1986 - 1991 Sampling at Selected Pharmaceutical Manufacturers

Between 1986 and 1991, EPA conducted sampling episodes at 13 pharmaceutical manufacturing facilities to: 1) characterize the pollutants in the wastewater being discharged at direct and indirect discharging facilities, 2) collect pollutant treatment system performance data from facilities with well-operated biological treatment systems (those systems attaining better than BPT annual average effluent levels), and 3) obtain treatability data from steam stripping and distillation.

Prior to 1986, the Agency had focused on 5 conventional pollutants and 126 priority pollutants identified in the 1977 Consent Decree. In 1986, the Agency expanded the analysis of pharmaceutical manufacturing wastewater and wastewater treatment sludges to determine the presence and levels of all the pollutants on the "Industrial Technology Division (ITD) List of Analytes" (hereinafter, the "List of Analytes").

The List of Analytes was derived from the "ITD/RCRA List of Lists" (8) using the following criteria:

- All analytes on the List of Lists were included on the List of Analytes, except:
  - -- Analytes which only appear on the "Acutely Toxic Chemicals" List in EPA's Chemical Emergency Preparedness Program (VTOX list);
  - -- Analytes which hydrolyze or are destroyed by water;
  - -- Analytes which are designated for analysis solely by high performance liquid chromatography (HPLC);

-- Analytes which must be analyzed by a subset of their chemical structure, or derivatized (except for the phenoxy acid herbicides which are analyzed by Method 615); and

-- Analytes for which no analytical standard is available.

- For analytes which hydrolyze, the hydrolysis product is included (if an analysis type and standard are available).

- Metal salts are included as the metal (e.g., beryllium, iron, sodium) and as the anion (e.g., F-, S-, CN-).

When the List of Analytes was first assembled in 1986, it contained 377 analytes.(9) The List of Analytes was expanded as the need to identify different analytes in the wastewater of different industries increased. The most recent List of Analytes was published again in 1990 and included 458 analytes.(10)

The List of Analytes was modified in the 1986-1991 sampling programs conducted for the pharmaceutical manufacturing industry to account for two program-specific needs:

1. After the first two sampling episodes (Nos. 1108 and 1111), EPA determined that it was not necessary to continue analyzing pharmaceutical manufacturing wastewater and wastewater treatment plant sludges for pesticides/herbicides (Method 1618) and dioxins/furans (Method 1613) unless the presence of these analytes was known or suspected. Pesticides/herbicides and dioxins/furans were not detected during the first two sampling episodes.

2. Analysis of volatile organic pollutants not on the List of Analytes was conducted on a site-specific basis after an assessment of the pre-sampling site visit information (i.e., information on solvent use by the pharmaceutical manufacturing facility). Pharmaceutical manufacturing industry wastewaters were characterized for additional analytes such as: ethanol, ethyl acetate, formaldehyde, isopropanol, isopropyl acetate, methanol, methyl formate, and petroleum naphtha.

During the sampling program, EPA gathered analytical data to characterize the wastewater from five direct dischargers and eight indirect dischargers. Treatment system performance data were gathered from three advanced biological treatment systems and two biological pretreatment systems. Treatment unit performance data documenting the performance of five steam stripping columns were gathered. The performance of one resin adsorption column and one cyanide destruction unit was also documented. Table 3-1 summarizes the types of facilities sampled and types of information collected.

Prior to each sampling episode, a presampling site visit was conducted to gather information on manufacturing operations, solvent usage, wastewater treatment systems, and possible sample point locations. Following each visit, a site visit report was prepared which documented the information gathered and provided recommendations regarding sample point locations. These site visit reports are included in the Record of this rulemaking.

A draft sampling plan was prepared before each sampling episode to document the procedures to be followed by the sampling crew during that episode. Prior to the sampling event, EPA sent the sampling plan to plant personnel for their review and comment. During the sampling episodes, sampling teams collected, preserved, and shipped the samples to an EPA-contracted laboratory according to established protocols defined in the sampling plan. EPA offered to split samples with facility personnel during all episodes.

Following each sampling episode, a sampling episode report was prepared to document facility manufacturing operations, sampling procedures followed, and analytical results obtained (including a QA/QC evaluation of these results), and also to provide a discussion of wastewater treatment plant operation and performance. Sampling plans and reports are also included in the Record of this rulemaking.

QA/QC evaluations of analytical data began at EPA's Sample Control Center (SCC) when the data were received from the contract laboratories. The raw data from the laboratories were reviewed for acceptability based on predefined data quality objectives specified in the respective analytical methods. The following objectives were reviewed:

- Sample completeness;
- Holding times;
- Calibration verification;
- Blanks;
- Matrix spikes;
- Matrix spike duplicates;
- Laboratory control samples; and
- ICP serial dilution.

After the above-mentioned criteria were reviewed by SCC, a data quality report was issued for each dataset. Datapoints deemed unacceptable by SCC were deleted from the dataset. Once the analytical data review was completed, a review was conducted to determine the following:

- The relative percent differences between split sample results;
- The ability to reproduce blind field duplicates; and
- Any significant deviations or upsets in process operations during the sampling event that may have impacted the results obtained.

Data not meeting QA/QC objectives with respect to blind field duplicates established by EPA for the analytical methods used were discussed in the respective sampling episode reports, and the impacted data were identified and deleted from the final database as appropriate.

3.2.4 Pharmaceutical Industry Questionnaires

The Pharmaceutical Manufacturing Industry Questionnaire distributed by EPA under authority of Section 308 of the Clean Water Act is a major source of data and information used in the development of effluent limitations guidelines and standards for the pharmaceutical manufacturing industry. This questionnaire requested information on:

- Pharmaceutical products and production processes;
- Chemical use and disposition;
- Wastewater treatment system design and operation parameters;
- Waste minimization/pollution prevention techniques;
- Wastewater characterization, including long-term self-monitoring data; and
- Financial and economic data for use in assessing economic impact and achievability of regulatory options.

EPA used a two-phase questionnaire approach to collect industry information including a screener questionnaire and a detailed questionnaire. The industry trade association PMA (now known as PhRMA) participated in the development of these questionnaires and both questionnaires were submitted to OMB for clearance. The screener questionnaire was distributed by EPA in May 1989 to 1,163 known or suspected pharmaceutical manufacturers. The screener questionnaire mailing list was developed after an extensive review of these sources:

- EPA current list of pharmaceutical manufacturers (respondents of the 308 Portfolio Survey in 1977 and 1979);
- List of pharmaceutical manufacturers maintained by Noyes Data Corporation (11);

- List of pharmaceutical manufacturers presented in the Physician's Desk Reference (12);
- List of pharmaceutical manufacturers presented in the Merck Index (13);
- List of facilities classified under SIC codes 2831, 2833, and 2834 in Dunn and Bradstreet's "Electronic Yellow Pages" (14);
- List of facilities classified under SIC codes 2831, 2833, and 2834 in Dunn and Bradstreet's World Marketing Directory (15);
- List of facilities classified under SIC codes 2831, 2833, and 2834 in the EPA Permit Compliance System (PCS);
- List of facilities classified: 1) as pharmaceutical manufacturers, or 2) under SIC codes 2831, 2833, and 2834 by state and/or regional wastewater permitting authorities; and
- List of pharmaceutical manufacturers published in the American Medical Association's Drug Evaluations.(16)

The screener questionnaire was designed to identify those facilities that could possibly be subject to the revised BPT, BAT, BCT, and PSES effluent limitations guidelines and standards. Detailed Questionnaires were then sent to pharmaceutical manufacturing facilities that were identified as: 1) direct dischargers of process wastewater involved in fermentation, natural extraction, chemical synthesis, or mixing, compounding, or formulating operations, or 2) indirect dischargers of process wastewater that potentially use solvents in the manufacturing process. Indirect dischargers that indicated in the screener that they use fermentation, extraction, or chemical synthesis process operations were assumed to potentially use solvents and were sent detailed questionnaires. In addition, the Detailed Questionnaire was sent to indirect dischargers utilizing mixing/ compounding/formulating operations if the facility indicated in the screener that they used solvents in these operations. The Detailed Questionnaire was not sent to facilities reporting zero discharge or research only operations in the screener questionnaire.

EPA wanted to ensure that the questionnaire was designed to collect representative data from the industry in the form that the industry maintains the data. Therefore, specific pharmaceutical manufacturers, as well as their trade association (PMA), were involved in the development of the Detailed Questionnaire. The PMA was given copies of the original draft of the survey, as well as subsequent drafts that included significant revisions or modifications.

In 1989, nine plants (six PMA members and three non-PMA members) were sent the Detailed Questionnaire as part of the pretest program. However, one facility closed prior to receiving the questionnaire, and a second declined to participate in the pretest program. Industry comments from the remaining seven facilities were incorporated into the survey, and a revised version was prepared.

As required by the Paperwork Reduction Act, (44 U.S.C. 3501 et seq.), EPA submitted the Detailed Questionnaire to the Office of Management and Budget (OMB) for review, and published a notice in the Federal Register that the questionnaire was available for review and comment.(17) In August 1990, OMB granted clearance of the technical section (Part A) and company-level financial information (Part B) of the Detailed Questionnaire. OMB denied clearance of questions asking for facility-specific economic information because industry claimed that this information was not readily available because of standard accounting practices used by the industry, was highly sensitive, and was not useful in developing effluent limitations guidelines, and therefore should not be required. Because the Agency considered facility-level financial data critical to the economic analysis, EPA pursued negotiations with OMB and industry to obtain full clearance for the questionnaire. These negotiations resulted in an agreement and clearance of the Part B of the questionnaire on July 15, 1991. This agreement allowed the questionnaire respondents to have the option of certifying certain conditions about the economic impacts that will result from costs incurred to comply with the effluent limitations guidelines and standards that EPA ultimately promulgates pursuant to this rulemaking. This facility impact certification. signed by an official of the owner company

with sufficient decision-making authority for this certification to be legally binding, could be submitted to EPA in lieu of completing the facility-level financial data in the Detailed Questionnaire.

In September 1991, EPA sent the Detailed Questionnaire to 280 facilities. This group included all direct dischargers involved in fermentation, extraction, chemical synthesis, or mixing, compounding, or formulating operations, all indirect dischargers involved in fermentation, extraction, and chemical synthesis operations, and a statistical sampling of indirect discharging facilities conducting mixing, compounding, or formulating operations that used solvents in their pharmaceutical manufacturing operations.

Not all indirect dischargers that performed mixing, compounding, or formulating operations were sent a Detailed Questionnaire because of the many similarities in production methods, wastewater volume and strength, and treatment operations used among this group of facilities. The variation in the questionnaire responses from this group of facilities was expected to be very small based on the information from the screener questionnaire supplied by this group of facilities. Consequently, a randomly selected subset of mixing, compounding, or formulating facilities that used solvents was surveyed. The random sample was developed using a methodology that ensured that the Detailed Questionnaire was distributed to facilities within four plant size groups, based on number of employees.(18)

Of the 280 facilities sent the Detailed Questionnaire, 245 were not closed or exempted and were deemed eligible to respond. Of the remaining 35 plants, 12 were closed and 23 were exempted from completing the questionnaire by EPA because they certified that they no longer manufactured pharmaceutical products and they had no plans to manufacture them in the future. EPA received responses from 244 of the 245 eligible facilities (a 99.6% response rate).

The Detailed Questionnaire was designed to gather data and information to develop revised BAT, BPT, and BCT effluent limitations guidelines and pretreatment standards (PSES, PSNS) intended to control priority and nonconventional volatile organic pollutants and any other conventional, priority and nonconventional pollutants of concern found in significant quantities (i.e., treatable concentrations). The Detailed Questionnaire gathered information on pharmaceutical production, chemical use and disposition, waste minimization and pollution prevention, wastewater generation, collection, and conservation, wastewater treatment, steam stripping, wastewater characteristics and economic financial data.(19)

The Agency required product-specific information to better understand the industry discharge pattern for individual pollutants.

The section on chemical use and disposition focused on a specific list of chemicals and compounds identified as associated with the pharmaceutical manufacturing industry. The specific list of 139 pollutants was created after review of the data and information sources then available were reviewed to determine all priority and nonconventional pollutants that were known or suspected to be used in the manufacture of pharmaceuticals. The list of 139 included pollutants meeting at least one of the following criteria:

- Identified by the 1975 and/or 1985 OAQPS solvent use and disposition data as being discharged in pharmaceutical manufacturing industry wastewaters;
- Identified by the pharmaceutical product patent search as potentially being used in pharmaceutical manufacture;
- Detected in the wastewaters of the pharmaceutical manufacturing industry;
- Identified as a volatile organic pollutant contained on the DSS list of analytes;

- Identified as a volatile organic pollutant on the ITD List of Analytes; or

- Identified as a volatile organic pollutant that was present in pharmaceutical manufacturing industry wastewaters according to the TRI database.

The Agency used the information on chemical use and disposition to provide wastewater loading estimates for various pollutants and to evaluate individual chemical usage by pharmaceutical manufacturers. In addition, EPA's Office of Air Quality Planning and Standards (OAQPS) evaluated the chemical emission information in support of its development of emission standards for hazardous air pollutants as required by the Clean Air Act. The Agency's Office of Pollution and Prevention (OPP) also evaluated the responses to determine the extent to which individual chemicals are recycled and reused.

Pollution prevention information on the extent to which source reduction and recycling is practiced in the pharmaceutical industry has been incorporated into EPA's regulatory development efforts to identify pollution prevention practices which have the potential for success.

Responses to questions pertaining to wastewater generation and collection have been used by EPA to characterize wastewater generation by the industry and to develop appropriate plant-by-plant treatment costs for process wastewater. EPA has used the information on wastewater treatment present at pharmaceutical facilities to determine the basis for revised regulations and to develop regulatory option costs. The information about the design and operating characteristics of in-place technology was also used for establishing technology basis of the regulatory options considered and for cost estimating purposes. In addition, the existing wastewater treatment information was used to estimate air emissions from the treatment of pharmaceutical manufacturing wastewaters.

The Agency realizes that steam stripping technology is being used by some pharmaceutical manufacturing facilities primarily to recover volatile organic compounds from wastewater. Consequently, the Agency solicited data on steam strippers to categorize as accurately as possible those units in place at pharmaceutical manufacturing plants to identify their design and operating parameters. The information provided on steam stripping has been used by EPA to evaluate what constitutes BAT level steam stripping under the Clean Water Act, as well as MACT level steam stripping under the Clean Air Act.

Conventional wastewater characteristics, including long-term performance averages supported by individual data points, were used by the Agency to develop revised limitations and standards for conventional pollutants. The Agency requested organics data to confirm the presence of priority and nonconventional pollutants that were expected in discharges of pharmaceutical manufacturing processes and to provide a source of treatment performance data for EPA's regulatory development.

The Agency used economic and financial data collected with the questionnaire to evaluate the economic impact of proposed regulations on the industry and to determine whether PSNS/NSPS would create a barrier to entry for facilities wishing to enter into pharmaceutical manufacturing.

3.2.5 Industry-Supplied Data

Facilities that discharge wastewater directly to surface waters of the United States must have a National Pollutant Discharge Elimination System (NPDES) permit, which establishes effluent limitations for various pollutants and requires the plants to monitor the levels of such pollutants in their effluent (see Section 402 CWA, as amended, implemented by 40 CFR 121-125). POTWs also require facilities to monitor pollutant levels in their wastewater prior to discharge. Additionally, some facilities with treatment systems monitor intermediate points within the systems to check the efficiency of the

unit. EPA requested that copies of the effluent monitoring data collected by plants in 1990 be submitted as part of the response to the Detailed Questionnaire. Data from treatment systems using the technologies described in Section 7 were entered into a database to establish the treatment performance of those technologies.

Some facilities and POTWs provided additional data in response to a specific request by EPA or as follow-up to the data provided in their questionnaire or data gathered during a sampling episode. These additional data submittals are explained in the following paragraphs.

In addition to the data submitted by Plant 30701 in their Detailed Questionnaire response, an additional 20 months of self-monitoring data were submitted to EPA from that direct discharger. The data were submitted by plant personnel because they felt that the pharmaceutical production reported in their response to the 1988 pre-test questionnaire was below normal levels. EPA statisticians analyzed the original questionnaire data and the additional 20 months of data. Since no significant differences between the datasets were found, the two datasets were combined, and used in the wastewater characterization of the industry.

In 1991, under authority of Section 308 of the Clean Water Act, EPA requested that Facility 30542 provide six months' worth of data documenting the performance of their cyanide destruction unit. Personnel from Plant 30542 collected and analyzed influent and effluent samples from their batch cyanide destruction (hydrogen peroxide oxidation) unit for six months. These data were submitted to EPA in November of 1991, and were used in the development of effluent limitations guidelines and standards for cyanide based on cyanide destruction technology.

In March of 1989, EPA conducted concurrent sampling episodes at Facility 30977 and the POTW to which they discharged. After those sampling episodes, POTW personnel provided EPA with additional priority and nonconventional pollutant data as well as data

collected characterizing the wastewater discharged from Facility 30977. These data were ultimately used for wastewater characterization of the pharmaceutical manufacturing industry.

When personnel from Facility 30832 indicated that the data collected by EPA during a sampling episode in July of 1986 were not representative of their typical effluent, EPA requested from the POTW to which that facility discharged, copies of long-term data collected over a 12-month period. The data submitted by the POTW were added to EPA's database, and have been used to help characterize pharmaceutical manufacturing wastewaters. Based on comparison to the long-term data, the data collected during the sampling episode were judged not to be representative of typical operations at Facility 30832, and were not used in the development of effluent limitation guidelines and standards.

3.2.6 Air Stripping, Steam Stripping, and Distillation Pilot Studies

Between October and December 1991, bench-scale and pilot-scale tests were conducted by EPA to study: 1) air stripping technology for ammonia removal from pharmaceutical manufacturing plant final effluent, and 2) steam stripping technology for volatile organic pollutant removal from pharmaceutical manufacturing plant process wastewaters.

The air stripping and steam stripping pilot studies were conducted at a pharmaceutical manufacturing facility with fermentation, chemical synthesis, formulation, and research operations. The total facility effluent was used as the feed to the pilot-scale air stripping study. The objective of this study was to examine the feasibility of obtaining at least 90% ammonia removal using air stripping technology. The wastewater characterization and treatment performance from the pilot-scale study are described in more detail in Sections 5 and 8, respectively.

For the steam stripping study, three wastewater streams from the facility were selected for analysis. The objective of this study was to achieve the lowest practical concentrations of volatile organic contaminants in the treated effluent, and to collect sufficient data to document these concentrations. On-site pilot-scale testing was conducted for two of the three streams. Bench-scale testing of the third wastewater was conducted at a contractor's laboratory because there was insufficient wastewater volume available at the facility to run the steam stripping test on a pilot-scale basis. The wastewater characterization and treatment performance from the steam stripping study are described in more detail in Sections 5 and 8, respectively.

In September 1993, EPA conducted an on-site treatment performance study using a pharmaceutical manufacturing facility's existing distillation column that treated wastewaters containing methanol. The objective of the study was to define operating parameters which resulted in optimum removal of methanol and compounds with similar volatility from wastewater and to collect sufficient data to document this removal. Waste characterization and treatment performance of the distillation study are discussed in Sections 5 and 8, respectively.

3.2.7 Patent Reviews

To better characterize volatile organic pollutant usage in the pharmaceutical manufacturing industry, EPA reviewed all patents identified for the approximately 1,300 pharmaceutical active ingredients identified as being manufactured. In 1987 the patents were reviewed for solvents on the ITD List of Compounds. The patents were reviewed again in 1991 to identify all solvents potentially used by the industry (not just those on the ITD List of Compounds). These patent reviews provided information regarding which volatile organic pollutants were most likely used in the manufacture of pharmaceutical products, and identified the plants at which the volatile organic pollutants were being used. EPA used patent search information to support the

development of the List of Pollutants analyzed for sampling efforts and for questionnaire development.

3.2.8 POTW Survey

In 1993 EPA surveyed nine POTWs to investigate the effect that indirect discharging pharmaceutical manufacturing facilities had on the POTWs that received the wastewater. This survey contained questions about local limits or special conditions which apply to pharmaceutical manufacturing facilities and volatile or semivolatile organics which caused problems for POTWs. The POTWs were also asked to explain problems connected with discharges from pharmaceutical manufacturing operations which they felt needed to be addressed in national regulations, and to supply other information regarding pharmaceutical manufacturing facility discharges within the sewer district that bear on the need for pretreatment standards.

Substantive responses were received from six of the surveyed POTWs. The responding POTWs provided EPA with a list of the pollutants frequently found in their wastewater, details of problems that result when wastewaters containing slug loads of pollutants are discharged, comments on the structure of PSES, and monitoring requirements which would be helpful to POTWs. The detailed responses to the POTW survey are included in the Record for this rulemaking.

3.2.9 Toxic Release Inventory (TRI) Data

Facilities which manufacture or use in their process at least 25,000 pounds of a listed toxic chemical must submit the Toxic Chemical Release Inventory (TRI) Reporting Form as required by Section 313 of the Emergency Planning and Community Right-to-Know Act. This form, known as Form R, provides the public with information on the releases of listed toxic chemicals in their communities and provides EPA with information to determine the need for future regulations.(20) The quantities of both routine and

accidental releases of listed toxic chemicals must be reported, as well as the maximum amount of the listed toxic chemical on site during the calendar year and the amount contained in wastes transferred off site. The Agency reviewed the information provided by the TRIs for the years 1987 through 1990 to assist in characterizing the chemical use and wastewater discharges from the industry, and to investigate current trends in chemical use and disposition in the pharmaceutical manufacturing industry.

3.3 Overview of the Industry

This section provides an overview of the pharmaceutical manufacturing industry by presenting general information on the geographical locations of facilities, Standard Industrial Classification (SIC) code distribution, value of shipments and number of employees in the industry, and age of facilities.

3.3.1 Geographical Location of Manufacturing Facilities

According to the 1989 Pharmaceutical Screener Questionnaire and the 1990 Detailed Questionnaire, there are 304 pharmaceutical facilities with solvent use which discharge wastewater in 34 states and the Commonwealth of Puerto Rico. This number includes the 244 facilities which completed the Detailed Questionnaire and the 60 indirect dischargers with mixing, compounding, or formulating operations which did not receive the Detailed Questionnaire. The majority of pharmaceutical manufacturing facilities are located in the eastern half of the United States, with the highest concentration of facilities in New Jersey, New York, Pennsylvania, and Puerto Rico. A map of the United States with the number of pharmaceutical manufacturing facilities in each state (or commonwealth) is presented in Figure 3-1. Table 3-2 presents the number of pharmaceutical manufacturing facilities by state and EPA region, along with the percentage of total facilities in each state and EPA region, and the total number of employees in each EPA region.

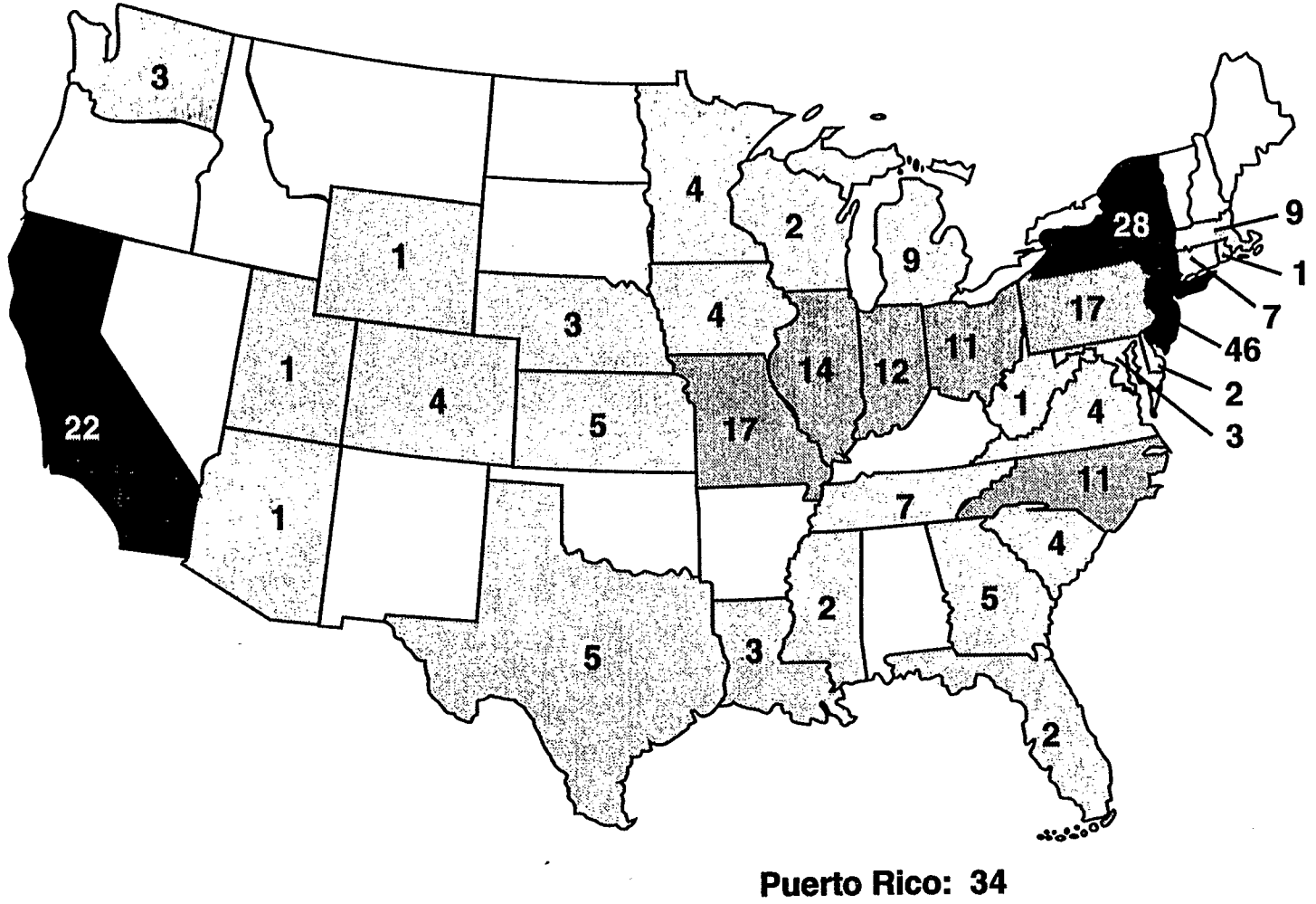

Figure 3-1. Location of Operating Pharmaceutical Facilities by State

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3.3.2 SIC Code Distribution

Standard Industrial Classification (SIC) codes, established by the U.S. Department of Commerce, are classifications of commercial and industrial establishments by the type of activity in which they engage. The primary purpose of SIC codes is to classify the manufacturing industries for the collection of economic data. An operating establishment is assigned an industry code on the basis of its primary activity, which is determined by its principal product or group of products. The principal product of a manufacturing establishment is determined by the value of production. Pharmaceutical manufacturing facilities generally cover SIC codes 2833, 2834, and/or 2836 (formerly 2831). Other products included under the definition of pharmaceutical manufacturing facilities are discussed in Section 3.4.

3.3.3 Value of Shipments and Number of Employees in the Industry

The Department of Commerce provided information on the value of shipments and the number of total employees in the pharmaceutical manufacturing industry by SIC code.(21) In 1991, the value of product shipments for SIC codes 2833, 2834, and 2836 were $6.25 billion, $37.4 billion, and $2.84 billion, respectively. In 1991, the total number of employees in the pharmaceutical industry for SIC codes 2833, 2834, and 2836 were 12,500, 129,100, and 12,100, respectively.

3.3.4 Age of Facilities

Table 3-3 presents a distribution of pharmaceutical manufacturing facilities by decade when operations began at the facility and when pharmaceutical manufacturing operations began at the facility. The majority of facilities which currently manufacture pharmaceuticals began such operations after 1960. The oldest reported pharmaceutical manufacturing operation began in 1879, while the most recent operation reported began in 1991.

3.4 Pharmaceutical Manufacturing Processes

The pharmaceutical manufacturing industry encompasses the manufacture, extraction, processing, purification, and packaging of chemical materials to be used as medication for humans and animals. For this rulemaking, EPA has defined the pharmaceutical manufacturing industry to include the manufacture of any of the following products:

- Biological products except diagnostic substances covered by the 1987 SIC Code 2836 (these products were formerly covered under the 1977 SIC Code 2831).
- Medicinal chemicals and botanical products covered by SIC Code 2833.
- Pharmaceutical products covered by SIC Code 2834.
- All fermentation, biological and natural extraction, chemical synthesis, and formulation products considered as pharmaceutically active ingredients by the Food and Drug Administration that are not covered by SIC Codes 2833, 2834, or 2836.
- Products with multiple end uses which are produced by a pharmaceutical manufacturing operation and used as a final pharmaceutical product, component of a pharmaceutical formulation, or as a pharmaceutical intermediate. Products which have non-pharmaceutical uses may also apply provided that the product was primarily intended for use as a pharmaceutical.
- Products not covered by SIC Codes 2833, 2834, and 2836 if they are produced by a pharmaceutical manufacturer by processes which generate wastewaters which closely correspond to those of pharmaceutical products.
- Cosmetic preparations covered by SIC Code 2844 which function as a skin treatment. (This group of preparations does not include products such as lipsticks or perfumes which serve to enhance appearance or to provide a pleasing odor, but do not provide skin care. In general, this excludes deodorants, manicure preparations, shaving preparations, and non-medicated shampoos which do not primarily function as a skin treatment.)

Products or activities specifically excluded from the pharmaceutical manufacturing category are:

- Surgical and medical instruments and apparatus covered by SIC Code 3841.
- Orthopedic, prosthetic, and surgical appliances and supplies covered by SIC Code 3842.
- Dental equipment and supplies covered by SIC Code 3843.
- Medical laboratories covered by SIC Code 8071.
- Dental laboratories covered by SIC Code 8072.
- In vitro diagnostic substances covered by SIC Code 2835.
- Diagnostic devices not covered by SIC Code 3841.
- Animal feeds which include pharmaceutically active ingredients such as vitamins and antibiotics. (The major portion of the product is nonpharmaceutical and the wastewater which results from the manufacture of feed is not characteristic of pharmaceutical manufacturing.)
- Foods and beverages which are fortified with vitamins or other pharmaceutically active ingredients. (The major portion of the product is nonpharmaceutical and the wastewater which results from the manufacture of these products is not characteristic of pharmaceutical manufacturing.)

Pharmaceutical research conducted at bench-scale, which does not fall within SIC Codes 2833, 2834, and 2836, does not appear to be a significant part of the industry from the point of view of effluent. In addition, this activity does not involve production and wastewater generation on a regular basis. However, in cases where the pharmaceutical research activity does involve the production of active ingredients at pilot-scale by processes generating wastewater which are similar to those in other subcategories, the

proposed effluent limitations guidelines contained in this development document are proposed to be used by permit writers and other interested parties.

3.4.1 Types of Pharmaceutical Processes and Products

There are four general types of manufacturing processes used by pharmaceutical manufacturing facilities. The four process types are: fermentation, biological and natural extraction, chemical synthesis, and mixing, compounding, or formulating. Figure 3-2 presents a bar graph of the number of facilities which use each type of manufacturing process. Table 3-4 presents examples of typical products from each type of manufacturing process.

3.4.2 General Process Descriptions

General process descriptions for each type of process operation are described in the following subsections. The specific processing steps on individual process lines may differ from these general descriptions as process operations will be tailored to the specific product being produced.

3.4.2.1 Fermentation

Most antibiotics and steroids are produced by the fermentation process, which involves three basic steps: inoculum and seed preparation, fermentation, and product recovery. Production of a fermentation pharmaceutical begins in the seed preparation step with spores from the plant master stock. The spores are activated with water, nutrients, and warmth; they are then propagated through the use of agar plates, test tubes, and flasks until enough mass is produced for transfer to the seed tank. In some fermentations, a single seed tank may provide inoculum for several fermentations. In this type of operation, the seed tank is never emptied completely, so the remaining seed serves as

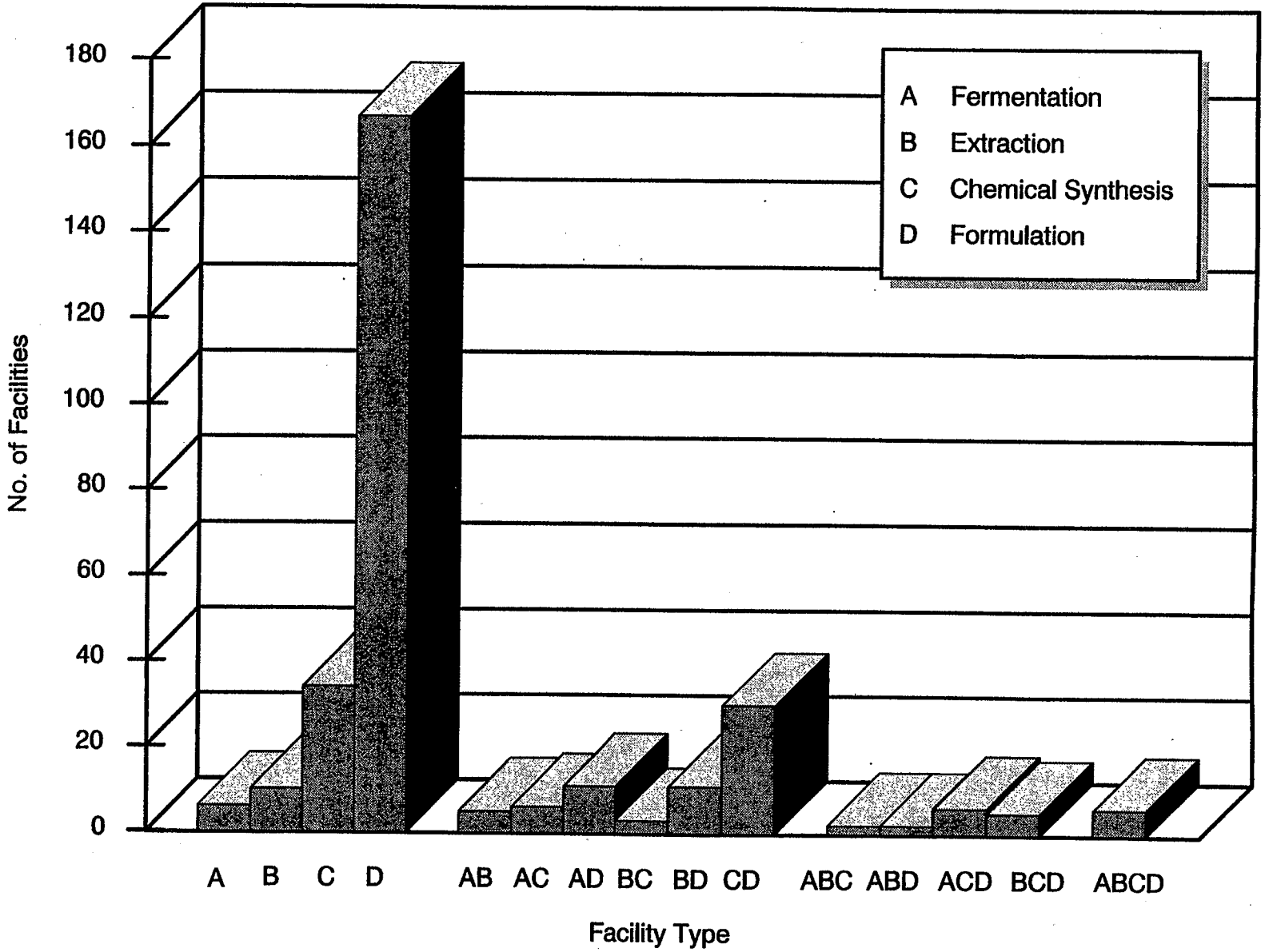

Figure 3-2. Number of Facilities in Each Combination of Pharmaceutical Manufacturing Types

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the inoculum for the next batch. The seed tank is emptied, sterilized, and reinoculated only when contamination occurs.

Fermentation is conventionally a large-scale batch process. The fermentation step begins with a water wash and steam sterilization of the fermenter vessel. Sterilized nutrient raw materials in water are then charged to the fermenter. Microorganisms grown from seed to aid in the fermentation process are transferred to the fermenter from the seed tank and fermentation begins. During fermentation, air is sparged into the batch and temperature is carefully controlled. After a period that may last from 12 hours to one week, the fermenter batch whole broth is ready for filtration. Filtration removes mycelia (i.e., remains of the microorganisms), leaving the filtered aqueous broth containing product and residual nutrients that are ready to enter the product recovery phase.

There are three common methods of product recovery: solvent extraction, direct precipitation, and ion exchange or adsorption. Solvent extraction is a recovery process in which an organic solvent is used to remove the pharmaceutical product from the aqueous broth and form a more concentrated solution. With subsequent extractions, the product is separated from any contaminants. Further removal of the product from the solvent can be done by either precipitation, solvent evaporation, or further extraction processes. Normally, solvents used for product recovery are recovered and reused. However, small portions left in the aqueous phase during the solvent "cut" can appear in the plant's wastewater stream. Based on information from the Detailed Questionnaire, the solvents most often used in fermentation operations are acetone, methanol, isopropanol, ethanol, amyl alcohol, and MIBK. Table 3-5 lists solvents used in fermentation operations.

Direct precipitation using heavy metal precipitating agents is another common method of product recovery. The method involves first precipitating the product as a metal salt from the aqueous broth, then filtering the broth, and finally extracting the product from the solid residues. Copper and zinc are priority pollutant metals known to be used in the precipitation process.(2)

Ion exchange or adsorption involves removal of the product from the broth, using solid materials such as ion exchange resin, adsorptive resin, or activated carbon. The product is recovered from the solid phase using a solvent, then recovered from the solvent by evaporation.

Occasionally, a fermentation batch becomes infested with a phage, a virus that attacks microorganisms necessary to the fermentation process. Phage infection is rare in a well-operated plant, but when it occurs, the plant may discharge very large amounts of wastewater in a short period of time because of the decontamination process. Typically, the infested batch is discharged early, and its nutrient pollutant concentration is higher than that of spent broth.

Steam is the major sterilizing medium for most equipment. However, detergents and disinfectants, to the extent that they are used, can contribute to waste loads. An example of a commonly used chemical disinfectant is phenol, a priority pollutant. Air pollution control equipment sometimes installed to clean fermentation waste off-gas is another wastewater source. The air and gas vented from the fermenters usually contain odoriferous substances (e.g., oxides of nitrogen and sulfur) and large quantities of carbon dioxide. Treatment is often necessary to deodorize the gas before release to the atmosphere. Some plants use incineration methods; others use liquid scrubbers. The blowdown from scrubbers may contain absorbed chemicals, soluble organic compounds, and insoluble organic oils and waxes.

Spent fermentation broth contributes pollutants to wastewater from the food materials contained in the broth, such as sugars, starches, protein, nitrogen, phosphate, and other nutrients. Fermentation wastes are very amenable to biological treatment. The spent broth can be satisfactorily handled by biological treatment systems in a concentrated form. Equalizing the broth prior to treatment helps avoid system upsets that may occur if the biota receive too high feed concentrations at one time.

Data from the Detailed Questionnaire generally show that process wastewater from fermentation plants is characterized by high BOD_5, COD, and TSS concentrations; relatively large flows; and a pH range of approximately 4.0 to 8.0.

3.4.2.2 Biological and Natural Extraction

Many materials used as pharmaceuticals are derived from such natural sources as the roots and leaves of plants, animal glands, and parasitic fungi. These products have numerous and diverse pharmaceutical applications, ranging from tranquilizers and allergy-relief medications to insulin and morphine. Also included in this group is blood fractionation, which involves the production of plasma and its derivatives.

Despite their diversity, all extractive pharmaceuticals have a common characteristic: they are too complex to synthesize commercially. They are either very large molecules, and/or their synthesis results in the production of several stereoisomers, only one of which has pharmacological value. Extraction is an expensive manufacturing process which requires collecting and processing large volumes of specialized plant or animal matter to produce small quantities of products. Facilities utilize extraction when there are no other reasonable alternatives for producing a desired active ingredient.

The extraction process consists of a series of operating steps beginning with the processing of a large quantity of natural or biological material containing the desired active ingredient. After almost every step, the volume of material being handled is reduced significantly. In some processes, reductions may be in orders of magnitude, and complex final purification operations may be conducted on quantities of materials only a few thousandths of the volume handled in earlier steps. Neither continuous processing methods nor conventional batch methods are suitable for extraction processing. Therefore, a unique assembly-line, small-scale batch processing method is used. Material is transported in portable containers through the plant in 75- to 100-gallon batches. A continuous line of containers is sent past a series of operating stations. At each station,

operators perform specific tasks on each batch in turn. As the volume of material being handled decreases, individual batches are continually combined to maintain reasonable operating volumes, and the line moves more slowly. When the volume is reduced to a very small quantity, the containers also become smaller, with laboratory-size equipment used in many cases. An extraction plant may produce one product for a few weeks; then, by changing the logistical movement of containers and redefining tasks to be conducted at each station, the plant can convert to the manufacture of a different product.

Residual wastes from an extraction plant essentially will be equal to the weight of raw material, since the active ingredients extracted are generally present in the raw materials at very low levels. Solid wastes are the greatest source of the pollutant load; however, solvents used in the processing steps can cause both air and water pollution. Detergents and disinfectants used in equipment cleaning operations are normally found in the wastewater.

Priority pollutants, including methylene chloride, toluene, chloroform, 1,2-dichloroethane, and phenol, were identified as being used in the manufacturing of extractive pharmaceuticals in the Detailed Questionnaire. The cations of lead and zinc are known to be used as precipitating agents. Phenol was identified as a disinfecting chemical. The other priority pollutants found were used as processing solvents. The Detailed Questionnaire identified nonconventional pollutants most often used in the extractive manufacturing process as ethanol, methanol, n-amyl acetate, isopropanol, and acetone. These nonconventional pollutants may be used as processing solvents. Table 3-6 lists solvents used in biological or natural extraction operations.

Solvents are used in two ways in extraction operations. Some solvents are used to remove fats and oils that would contaminate the products. These "defatting" extractions use an organic liquid that dissolves the fat but not the product material. Solvents are also used to extract the product itself. For example, when plant alkaloids are treated

with a base, they become soluble in such selected organic solvents as benzene, chloroform, and 1,2-dichloroethane.

Ammonia is used in many extraction operations because it is necessary to control the pH of water solutions from both animal and plant sources to separate valuable components from waste materials. Ammonium salts are used as buffering chemicals, and aqueous or anhydrous ammonia is used as an alkalinizing reagent. The high degree of water solubility of ammonium salts prevents unwanted precipitation of salt, and they do not react chemically with animal or plant tissue. Such basic materials as hydroxides and carbonates of alkali metals do not have these advantages.

The principal sources of wastewater from biological/natural extraction operations are: (1) spent raw materials (e.g., waste plasma fractions, spent media broth, plant residues); (2) floor and equipment wash water; (3) chemical wastes (e.g., spent solvents); and (4) cleanup of spills.

Wastewater from extraction plants is generally characterized by low BOD_5, COD, and TSS concentrations; small flows; and pH values of approximately 6.0 to 8.0.

3.4.2.3 Chemical Synthesis

Most of the active ingredients marketed and sold as drugs are manufactured by chemical synthesis. Chemical synthesis is the process of manufacturing pharmaceuticals using organic and inorganic chemical reactions. Since most of these compounds are produced in batch operations, the conventional batch reaction vessel is the major piece of equipment used on the process line.

The reaction vessel is one of the most standardized equipment designs in the industry. Generally, it is made of either stainless steel or glass-lined carbon-steel, and it contains a carbon-steel outer shell suitable for either cooling water or steam. Inside the vessel is a

motor-driven agitator and a baffle. Vessels of this type are made in many different sizes, with capacities ranging from 0.02 to 11.0 m^3 or more.

The basic vessels may be fitted with different attachments depending on the process needs of the product to be manufactured. Baffles usually contain sensors to measure the temperature of the reactor contents. Dip tubes may be used to introduce reagents into the vessels below the liquid surface. The vessel's agitators may be powered by two-speed motors or by variable-speed motor drives. The reactor may be mounted on load cells to accurately weigh the reactor contents. The batch reactors are typically installed with only the top heads extending above the plant operating floor to provide the operator with easy access for loading and cleaning. Also, one of the top nozzles may be fitted with a floodlight and another with a glass cover to enable an operator to observe the reactor contents.

The reactors can be modified for additional uses. By using heating or refrigeration devices, the chemicals may be boiled or chilled in them, according to process needs. By adding reflux condensation equipment, the vessel may perform complete reflux operations (i.e., recycling of condensed vapors). The vessels can also become evaporators if vacuum is applied. The reactors may also be used to perform solvent extraction operations and, by operating the agitator at a slow speed, the vessels can serve as crystallizers.

Synthetic pharmaceutical manufacture consists of using one or more of these reactor vessels to perform, in a step-by-step fashion, the various operations necessary to make the product. Following a definite recipe, the operator (or, increasingly, a programmed computer) adds reagents; increases or decreases the flow rate of cooling water, chilled water, or steam; and starts and stops pumps which transfer the reactor contents to another vessel. At appropriate steps in the process, solutions are pumped either through filters or centrifuges, or into solvent recovery headers or waste sewers.

The reactor vessels with an assembly of auxiliary equipment are usually arranged into independent process units, which are suitable for the complete or partial manufacture of many different pharmaceutical compounds. Only with the highest volume products is the process unit "dedicated" to manufacturing only one product. Large pharmaceutical plants may have many such units, while smaller plants may have only one or two.

Each pharmaceutical product is usually manufactured in a "campaign," in which one or more process units are used for a few weeks or months to manufacture enough compound to satisfy the projected sales demand. Campaigns are usually tightly scheduled, with detailed coordination extending from procurement of raw materials to packaging and labeling of the product. For a variable period of time, a process unit actively manufactures a specific compound. At the end of the campaign for one product, another is scheduled to follow. After equipment cleaning, the same equipment is then used to make a completely different product, using different raw materials, executing a different recipe, and creating different wastes.

A variety of priority pollutants are used as reaction and purification solvents during chemical synthesis. According to the Detailed Questionnaire, priority pollutants used by facilities during the chemical synthesis process include benzene, chlorobenzene, chloroform, chloromethane, o-dichlorobenzene, 1,2-dichloroethane, methylene chloride, phenol, toluene, and cyanide.

The Detailed Questionnaire identified the top five nonconventional pollutants associated with chemical synthesis as methanol, acetone, isopropanol, ethyl acetate, and ethanol. Six-member ring compounds, such as xylene, pyridine, and toluene, are also widely used organic solvents because they are stable compounds that do not easily take part in chemical reactions. These compounds are used either in the manufacture of synthesized pharmaceuticals or are produced as the result of unwanted side reactions. Table 3-7 lists solvents used in chemical synthesis operations.

Solvents are used in chemical synthesis processes to dissolve gaseous, solid, or viscous reactants in order to bring all the reactants into close molecular proximity. Solvents also serve to transmit heat to or from the reacting molecules. By physically separating molecules from each other, solvents slow down some reactions that would otherwise take place too rapidly, resulting in unwanted side reactions and excessive temperature increases.

Some solvents are also used to control the reaction temperature. It is common practice in a batch-type synthesis to select a solvent which is compatible with the reaction and which has a boiling point the same as the desired reaction temperature. Heat is then applied to the reaction mass at a rate sufficient to keep the mixture boiling continuously. Vapors that rise from the reaction vessel are condensed, and the liquefied solvent is allowed to drain back into the reaction vessel. This refluxing prevents both overheating and overcooling of the reactor contents, and can automatically compensate for variations in the rate of release or absorption of chemical energy.

Many plants operate solvent recovery units that purify contaminated solvents for reuse. These units usually contain distillation columns, and may also include solvent/solvent extraction operations in which a second solvent is used to separate impurities. These operations may result in aqueous wastes that contain residues fully or partially saturated with residual solvent.

Wastewater is generally produced with each chemical modification that requires filling and emptying the batch reactors. This wastewater can contain unreacted raw materials, as well as some solvents, along with a large number of compounds that differ due to the varied chemical reactions performed (e.g., nitration, amination, halogenation, sulfonation, alkylation). Chemical synthesis effluent generally has a high BOD_5 and COD waste load.

The pollutants in chemical synthesis wastewater vary with respect to toxicity and biodegradability. The production steps may generate acids, bases, cyanides, metals, and

other pollutants, while the waste process solutions and vessel wash water may contain residual organic solvents. Occasionally, chemical synthesis wastewater is incompatible with biological treatment systems because it is too concentrated or too toxic for the biomass in the treatment system. Thus, it may be necessary to equalize and/or chemically pretreat some chemical synthesis wastewater prior to biological treatment.

Primary sources of wastewater from chemical synthesis operations are: (1) process wastes such as spent solvents, filtrates, and concentrates; (2) floor and equipment wash water; (3) pump seal water; (4) wet scrubber wastewater; and (5) spills. Wastewater from chemical synthesis plants can be characterized as having high BOD_5, COD, and TSS concentrations; large flows; and extremely variable pH values, ranging from 1.0 to 11.0.

3.4.2.4 Mixing, Compounding, or Formulating

Pharmaceutically active ingredients are generally produced by batch processes in bulk form and must be converted to dosage form for consumer use. Common dosage forms for the consumer market are tablets, capsules, liquids, and ointments. In addition, active ingredients can also be incorporated into patches and time release capsules.

Tablets are formed in a tablet press machine by blending the active ingredient, filler, and binder. The filler (e.g., starch, sugar) is required to dilute the active medicinal ingredient to the proper concentration, and a binder (e.g., corn syrup or starch) is necessary to bind the tablet particles together. A lubricant (e.g., magnesium stearate) may be added for proper tablet machine operation. The dust generated during the mixing and tableting operation is collected and usually recycled directly to the same batch, while broken tablets generally are collected and recycled to the granulation operation in a subsequent lot. Some tablets are coated by tumbling with a coating material and then dried. After the tablets have been coated and dried, they are sent to the packaging unit where they are bottled. Tablet-coating operations can be a significant

source of air emissions of solvents if solvent-based coatings are used, and can contribute solvents to the plant wastewater if certain types of air pollution control equipment (wet scrubbers or activated carbon) are used to capture solvent vapors from tablet-coating operations. Wastewater from the wet scrubber is likely to be sewered as is the condensate from the steam used to regenerate the activated carbon.

The first step in capsule production is to form a hard gelatine shell. The shells are produced by machines that dip rows of rounded metal dowels into a molten gelatine solution, and then strip the capsules from the dowels after the capsules have cooled and solidified. Imperfect capsules are remelted and reused, if possible, or sold for glue manufacture. Most pharmaceutical companies purchase empty capsules from a few specialty producers. The active ingredient and filler are mixed before being poured by machine into the empty gelatine capsules. The filled capsules are bottled and packaged. As in tablet production, some dust is generated, which is recycled to the production line.

Liquid preparations are formulated for injection or oral use. In both cases, the liquid active ingredient is first weighed and then dissolved in water. Injectable solutions are bulk-sterilized by heat or filtration and then poured into sterilized bottles. Oral liquid preparations can be bottled directly without the sterilization steps. Wastewater is generated by general cleanup operations, spills, and breakage.

Ointments are produced by blending an active ingredient(s) with an ointment base such as polyethylene glycol. The blended product is then poured into tubes by machine and packaged. Wastewater generated from these operations are all from equipment cleaning operations.

The primary objective of mixing, compounding, or formulating operations is to convert the manufactured products into a final, usable form. The necessary production steps typically have small wastewater flows because very few of the unit operations generate

wastewater. The primary use of water is in the actual formulating process, where it is used for cooling and for equipment and floor washing.

Wastewater sources from mixing, compounding, or formulating operations are: (1) floor and equipment wash water, (2) wet scrubbers, and (3) spills. The use of water to clean out mixing tanks can periodically flush dilute wastewaters of unusual composition into the plant sewer system. The washouts from mixing tanks may be used to prepare the master batches of the pharmaceutical compounds and may contain inorganic salts, sugars, and syrup. Other sources of contaminated wastewater are dust and fumes from scrubbers, either in building ventilation systems or on specific equipment. In general, this wastewater is readily treatable by biological treatment systems.

An analysis of the pollutant information in the pharmaceutical manufacturing database shows that wastewater from mixing, compounding, or formulating plants normally has low BOD_5, COD, and TSS concentrations; relatively small flows; and pH values of 6.0 to 8.0.

3.4.3 Pharmaceutical Manufacturing Process Variability

The wastewater effluent flow and composition from a typical pharmaceutical manufacturing facility can be highly variable. Factors contributing to such variability are:

- Campaigning;
- Batch processing; and
- Wastewater commingling.

Because many pharmaceutical products are manufactured in campaigns, most wastewater is generated during product changeover. The process equipment must be cleaned out to avoid product contamination. The composition of the wastewater will vary according to the products that were manufactured on that process line.

Pharmaceuticals are manufactured by batch and continuous manufacturing operations. Batch-type production is by far the most common manufacturing technique, as presented in the production operation breakdown in Table 3-8. Many pharmaceutical facilities conduct multiple batch operations, some in series and some concurrently. Often several of the required batch processes are performed at the same time in separate reactors, each with its own schedule. Each batch may have unique waste stream characteristics. In fermentation operations, it can take a few days to several weeks to complete the ferment, during which little or no wastewater is generated. However, during product recovery operations, high-volume, high-strength wastewaters are generated.

It is also common practice in the pharmaceutical manufacturing industry to commingle organic-contaminated wastewaters. In many cases commingling is necessary to collect sufficient wastewater volume to properly operate an economically sized treatment unit such as a steam stripper. Commingled wastes may be added to the treatment unit feed tank on a variable schedule, thus altering the feed composition on a real-time basis. In other cases, segregating for purposes of recovery and treatment may be appropriate and cost effective.

A variety of solvents are used in the pharmaceutical manufacturing industry and end up in the industry's wastewater. Many solvents are process-specific and cannot be interchanged in other pharmaceutical processes. In addition, solvents must be approved by the FDA for each process. FDA regulations require that before a change can be made to an approved process, industry must meet the requirements of product purity and product efficacy as specified in the FDA approval. Consequently, simplification of wastestream composition by chemical substitution to a common solvent may not be possible or desirable. Nonetheless, EPA has worked with the Food and Drug Administration (FDA) to incorporate pollution prevention into the proposed guidelines and standards. See Section 7.2.1.2 for a more detailed discussion of EPA and FDA efforts towards pollution prevention in the pharmaceutical industry.

3.5 Trends in the Industry

The "Preliminary Data Summary for the Pharmaceutical Point Source Category" (22) gives a snapshot of the pharmaceutical manufacturing industry in the late 1970s and the early 1980s. By comparing these pre-1986 sources to the data available in the 1989 Pharmaceutical Screener Questionnaire and the 1990 Detailed Questionnaire, trends in the manufacturing process types used by pharmaceutical manufacturing facilities, the treatment technologies used at pharmaceutical manufacturing facilities, and the chemicals used in their manufacturing processes were observed. These trends are described in the following subsections.

3.5.1 Manufacturing Process Types

Since 1986, the number of pharmaceutical manufacturing facilities engaging in fermentation has increased, while those engaging in biological or natural extraction has decreased. These trends are shown in the following table.

Type of Facility	Percentage of Facilities Using Process Prior to 1986	Percentage of Facilities Using Process in 1989/1990
Fermentation	7.8	14.5
Biological or Natural Extraction	17.0	14.5
Chemical Synthesis	29.3	30.3
Mixing, Compounding, or Formulating	80.0	80.0

The total of the percentages is not 100 because any one facility may manufacture multiple process types.

3.5.2 Treatment Technologies in Use

Table 3-9 presents the trends in wastewater treatment technologies used by pharmaceutical manufacturing facilities. Since 1986, the use of neutralization, equalization, activated sludge, primary clarification, multimedia filtration, steam stripping, secondary clarification, granular activated carbon, and oxidation have all increased, while the use of aerated lagoons, chlorination, waste stabilization ponds, and trickling filters have decreased slightly. Upward or downward trends cannot be assessed for settleable solids removal, primary sedimentation, polishing ponds, evaporation, dissolved air floatation, pH adjustment, or phase separation since data were not available for both pre-1986 and post-1986 time frames.

3.5.3 Chemical Substitution

The pharmaceutical manufacturing industry has decreased its use of many chemicals because of their toxicity and contribution to air and water pollution. Use of chlorinated compounds has decreased the most. Based on a review of TRI data for 1987-1990 from pharmaceutical manufacturing facilities, the average annual discharge of chloroform, methylene chloride, carbon tetrachloride, benzene, methyl isobutyl ketone, pyridine, and xylene has decreased between the years 1987 and 1990, whereas the average annual discharge of isopropanol, methyl cellosolve, and phenol has increased. Table 3-10 presents the amounts each compound has decreased or increased and the percent change.

Table 3-1

Facilities Sampled As Part of the Pharmaceutical Manufacturing Industry Study

Plant Code	Sampling Dates	Subcategory	Days Sampled	Stream Characterization	Technology Sampled			
					Biological	Steam Stripping	Resin Adsorption	Cyanide Destruction
1. Indirect Dischargers								
30618	04/19/86-04/21/86	A,B,C,D,E	2	X	--	--	--	--
30832	07/16/86-07/18/86	A,C,D,E	2	X	--	--	--	--
30759	07/29/86-07/31/86	A,B,C,D,E	2	X	X	--	--	--
30022	03/11/87-03/13/87	A,B,C,D,E	2	X	X	--	--	--
30918	05/10/88-05/12/88	A,B,C,E	2	X	--	--	--	--
30329	09/12/88-09/16/88	A,C,D,E	3	X	--	PC, FT, DP	--	--
30977	03/28/89-03/30/89	A,B,C,E	2	X	--	--	--	--
30618	06/05/89-06/09/89	A,B,C,D,E	4	--	--	PC	X	--
2. Direct Dischargers								
30010	02/25/87-02/27/87	C	2	X	X	--	--	--
30487	09/19/88-09/23/88	C	4	--	--	PC	--	--
30542	03/13/89-03/17/89	A,C,E	4	--	--	--	--	X
30623	04/03/90-04/13/90	A,C	10	X	X	--	--	--
30540	06/03/91-06/13/91	A,B,C,D,E	10	X	X	--	--	--

Notes: PC = packed column; FT = flash tank; DP = distillation pot.
Subcategory refers to the type of manufacturing operations performed at the facility.

Subcategory A = Fermentation
Subcategory B = Extraction
Subcategory C = Chemical Synthesis
Subcategory D = Formulation
Subcategory E = Research and Development

Table 3-2

Pharmaceutical Industry
Geographic Distribution(a)

Location	Number of Plants	Percentage of Total Plants	Total Number of Employees in Region
Eastern United States			
EPA Region I:			
Connecticut	7	2.3	
Maine	0	0.0	
Massachusetts	9	3.0	
New Hampshire	0	0.0	
Rhode Island	1	0.3	
Vermont	0	0.0	
EPA Region I Totals	17	5.6	7,025
EPA Region II			
New Jersey	46	15.1	
New York	28	9.2	
Puerto Rico	34	11.2	
Virgin Islands	0	0.0	
EPA Region II Totals	108	35.5	60,322
EPA Region III			
Delaware	2	0.7	
Maryland	3	1.0	
Pennsylvania	17	5.6	
Virginia	4	1.3	
West Virginia	1	0.3	
District of Columbia	0	0.0	
EPA Region III Totals	27	8.9	14,558

Table 3-2

(Continued)

Location	Number of Plants	Percentage of Total Plants	Total Number of Employees in Region
EPA Region IV			
Alabama	0	0.0	
Georgia	5	1.6	
Florida	2	0.7	
Mississippi	2	0.7	
North Carolina	11	3.6	
South Carolina	4	1.3	
Tennessee	7	2.3	
Kentucky	0	0.0	
EPA Region IV Totals	31	10.2	12,927
EPA Region V			
Illinois	14	4.6	
Indiana	12	4.0	
Ohio	11	3.6	
Michigan	9	3.0	
Wisconsin	2	0.7	
Minnesota	4	1.3	
EPA Region V Totals	52	17.1	37,235
Eastern U.S. Total (EPA Regions I-V)	**235**	**77.3**	**132,067**

Table 3-2

(Continued)

Location	Number of Plants	Percentage of Total Plants	Total Number of Employees in Region
Western United States			
EPA Region VI			
Arkansas	0	0.0	
Louisiana	3	1.0	
Oklahoma	0	0.0	
Texas	5	1.6	
New Mexico	0	0.0	
EPA Region VI Totals	8	2.6	2,121
EPA Region VII			
Iowa	4	1.3	
Kansas	5	1.6	
Missouri	17	5.6	
Nebraska	3	1.0	
EPA Region VII Totals	29	9.5	6,764
EPA Region VIII			
Colorado	4	1.3	
Utah	1	0.3	
Wyoming	1	0.3	
Montana	0	0.0	
North Dakota	0	0.0	
South Dakota	0	0.0	
EPA Region VIII Totals	6	2.0	1,252

Table 3-2

(Continued)

Location	Number of Plants	Percentage of Total Plants	Total Number of Employees in Region
EPA Region IX			
Arizona	1	0.3	
California	22	7.2	
Nevada	0	0.0	
Hawaii	0	0.0	
EPA Region IX Totals	23	7.6	9,520
EPA Region X			
Alaska	0	0.0	
Idaho	0	0.0	
Oregon	0	0.0	
Washington	3	1.0	
EPA Region X Totals	3	1.0	534
Western U.S. Total (EPA Regions VI-X)	**69**	**22.7**	**20,191**
U.S. Totals	**304**	**100**	**152,258**

(a) Employment obtained from the 1989 Screener Questionnaire. Facility locations obtained from the Detailed Questionnaire and the 1989 Screener Questionnaire.

Table 3-3

Distribution of Pharmaceutical Manufacturing Facilities by Date of Initiation of Operations(a)

Decade	Number of Facilities Reporting	
	Facility Operations Began	Pharmaceutical Manufacturing Operations Began
Prior to 1930s	19	10
1930s	6	5
1940s	14	14
1950s	17	18
1960s	26	27
1970s	47	46
1980s	50	57
1990s	4	5
No Response	61	62
Total	244	244

(a)Data obtained from 244 facilities responding to the Detailed Questionnaire.

Table 3-4

Example Pharmaceutical Products by Manufacturing Process and Classification

Fermentation Products	Extraction Products	Chemical Synthesis Products	Mixing/Compounding/ Formulating Products
Antibiotics	Antineoplastic Agents	Antibiotics	Cold Formulas
Amphotericin	Vinblastine	Aztreonam	Benedryl elixir
Chlortetracycline	Vincristine	Clindamycin	Dermatological Agents
Lincomycin	Enzymes and Digestive Aids	Antihistamines	Calamine
Nystatin	Pancreatin USP	Mecfizune dihydrochloride	Salicylic acid
Penicillin G	Papain	Cardiovascular Agents	Powders
Penicillin V	Central Depressants	Methyldopa	Desenex Powder
Streptomycin	Codene	Central Stimulants	Mouthwash
Vancomycin	Morphine Sulphate	Amitriptyline	Listerine
Antineoplastic Agents	Noscapine	Caffeine	Tablets and Capsules
Dextran	Thebaine	Central Depressants	Contact
Therapeutic Nutrients	Hematological Agents	Acetaminophen	Di-gel tablets
L-Lysine	Heparin	Aspirin (acetyl salicylic acid)	Accutane
Vitamins	Insulin	Hormones	Ointments
Ascorbic acid (C)	Vaccines	Cortisone acetate	Absorbine Jr.
Riboflavin (B2)	Strepvax II	Dexamethasone acetate	Lubriderm
Steroids		Fluorometholone	Caladryl
		Hydrocortisone	Vicks Vaporrub
		Testosterone	
		Vitamins	
		Niacinamide	

Table 3-5

Solvents Used in Fermentation Operations

Acetone	n-Heptane
Acetonitrile	n-Hexane
Ammonia (aqueous)	Isopropanol
n-Amyl acetate	Isopropyl acetate
Amyl alcohol	Methanol
n-Butyl acetate	Methyl cellosolve
n-Butyl alcohol	Methylene chloride
Chloroform	Methyl isobutyl ketone (MIBK)
N,N-Dimethylformamide	Petroleum naphtha
Ethanol	Phenol
Ethyl acetate	Toluene
Formaldehyde	Triethylamine

Table 3-6

Solvents Used in Biological or Natural Extraction Operations

Acetone	Ethylene glycol
Acetonitrile	Formaldehyde
Ammonia (aqueous)	n-Heptane
n-Amyl acetate	n-Hexane
Amyl alcohol	Isopropanol
n-Butyl alcohol	Isopropyl acetate
Chloroform	Isopropyl ether
1,2-Dichloroethane	Methanol
Diethylmine	Methylene chloride
Diethyl ether	Petroleum naphtha
N,N-Dimethylformamide	Phenol
Dimethyl sulfoxide	n-Propanol
1,4-Dioxane	Pyridine
Ethanol	Tetrahydrofuran
Ethyl acetate	Toluene

Table 3-7

Solvents Used in Chemical Synthesis Operations

Acetone	Formaldehyde
Acetonitrile	Formamide
Ammonia (aqueous)	Furfural
n-Amyl acetate	n-Heptane
Amyl alcohol	n-Hexane
Aniline	Isobutyraldehyde
Benzene	Isopropanol
2-Butanone (MEK)	Isopropyl acetate
n-Butyl acetate	Isopropyl ether
n-Butyl alcohol	Methanol
Chlorobenzene	Methylamine
Chloroform	Methyl cellosolve
Chloromethane	Methylene chloride
Cyclohexane	Methyl formate
o-Dichlorobenzene (1,2-Dichlorobenzene)	Methyl isobutyl ketone (MIBK)
1,2-Dichloroethane	2-Methylpyridine
Diethylamine	Petroleum naphtha
Diethyl Ether	Phenol
N,N-Dimethyl acetamide	Polyethylene glycol 600
Dimethylamine	n-Propanol
N,N-Dimethylaniline	Pyridine
N,N-Dimethylformamide	Tetrahydrofuran
Dimethyl sulfoxide	Toluene
1,4-Dioxane	Trichlorofluoromethane
Ethanol	Triethlyamine
Ethyl acetate	Xylenes
Ethylene glycol	

Table 3-8

Production Operation Breakdown(a)

Type of Operation	Number of Operations					Percent of Total Operation
	Manufacturing Processes				Total	
	Fermentation	Biological Extraction	Chemical Synthesis	Mixing/ Compounding/ Formulating		
Batch	309	189	1,059	3,675	5,232	99
Continuous	16	1	16	8	41	1
Total Number of Operations	325	190	1,075	3,683	5,273	100
Percent of Total Operations	6	4	20	70	100	
Percent of Subcategory Operations which are Batch	95	99	99	100	99	

(a) Production data obtained from 244 facilities responding to the Detailed Questionnaire.

Table 3-9

Trends in Treatment Technologies Used at Pharmaceutical Manufacturing Facilities(a)

Treatment Technology	Percentage of Facilities Using This Type of Treatment Technology Prior to 1986	Percentage of Facilities Using This Type of Treatment Technology in 1989/1990
Neutralization	26.0	44.3
Equalization	20.1	28.6
Activated sludge	16.9	20.5
Settleable solids removal	13.3	NA
Primary sedimentation	12.0	NA
Aerated lagoon	7.5	4.9
Primary clarification	3.9	9.8
Chlorination	3.6	2.5
Polishing ponds	3.2	NA
Waste stabilization pond	2.9	2.5
Trickling filter	2.9	2.0
Multimedia filtration	2.3	6.1
Steam stripping	1.9	5.7
Evaporation	1.9	NA
Secondary clarification	1.6	20.9
Granular activated carbon	1.3	3.3
Oxidation	1.0	2.0
Dissolved air flotation	1.0	NA
pH adjustment	NA	50.0
Phase separation	NA	12.3

The total of the percentages is not 100 because any one facility may have multiple treatment technologies and some facilities do not have treatment in place.

NA - Not available.

(a) Data obtained from reference 22 and the responses to the Detailed Questionnaire.

Table 3-10

Trends in Average Annual Discharges of Compounds Between the Years 1987 and 1990

Compound	Amount Increased or Decreased (lbs)	Percent Change
Chloroform	-1.2×10^6	-68
Methylene chloride	-10×10^6	-32
Carbon tetrachloride	-79,000	-65
Benzene	-63,000	-88
Methyl isobutyl ketone	-3×10^6	-58
Pyridine	-229,000	-49
Xylene	-1×10^6	-51
Isopropanol	+68,000	+83
Methyl cellosolve	+640,000	+102
Phenol	+49,000	+166

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SECTION 4

INDUSTRY SUBCATEGORIZATION

4.1 Introduction

The purpose of subcategorization is to group together facilities of similar characteristics so that effluent limitations guidelines and standards representative of each group can be developed. This provides each subcategory with a uniform set of effluent limitations guidelines which take into account technological achievability and economic impacts unique to that subcategory.

For this proposed rulemaking, EPA considered the following factors in the subcategorization of the pharmaceutical manufacturing industry:

- Manufacturing processes;
- Wastewater characteristics and treatability;
- Product types;
- Raw materials;
- Plant size;
- Plant age;
- Plant location;
- Nonwater quality environmental impacts; and
- Treatment costs and energy requirements.

After evaluating the above factors, the Agency determined that subcategorization of the pharmaceutical manufacturing industry is necessary. The results of these evaluations are presented in the following sections:

- Section 4.2 discusses the regulatory background of subcategorization in the pharmaceutical manufacturing industry;

- Section 4.3 presents the proposed subcategorization basis; and
- Section 4.4 presents conclusions.

4.2 Background

The original subcategorization scheme for the pharmaceutical manufacturing industry was published in the November 17, 1976 Federal Register.(1) This subcategorization scheme was based on the operations listed below:

- Subcategory A - Fermentation Operations
- Subcategory B - Biological and Natural Extraction Operations
- Subcategory C - Chemical Synthesis Operations
- Subcategory D - Mixing, Compounding, or Formulating Operations
- Subcategory E - Pharmaceutical Research Operations

Subsequently, EPA published proposed effluent limitations guidelines and standards for the pharmaceutical manufacturing industry in November 1982. As discussed in the preamble to the 1982 regulation, EPA proposed to combine Subcategories A through D above into a single subcategory.(2) Along with comments on the November 1982 proposal, EPA received additional influent and effluent conventional and nonconventional pollutant data. EPA statistically analyzed both new and existing influent and effluent conventional and nonconventional pollutant data for all direct dischargers to determine if the proposed change to create a single subcategory was appropriate. A detailed discussion of the data sources and the statistical comparisons used is presented in Section IV of the 1983 Final Development Document (3), and is summarized below.

The statistical comparisons of conventional pollutants and the nonconventional pollutant COD indicated that the subcategorization scheme should separate fermentation and chemical synthesis operations (Subcategory A and C) from extraction and mixing, compounding, or formulating operations (Subcategory B and D). The analyses showed

that the influent and effluent conventional pollutant and COD concentrations, as well as discharge flows, of facilities with Subcategory A and C operations are similar and that these same characteristics are similar between facilities with Subcategory B and D operations. These characteristics are different, however, between the Subcategory A and C facility group and the Subcategory B and D facility group. These differences indicated that different effluent discharge levels of conventional pollutants and COD would be expected when facilities in both groups used the same control technology. However, because the existing separate subcategories accommodated these differences and because permitting authorities and the regulated industry were familiar with that scheme, EPA decided to maintain the existing subcategorization scheme at that time.

Pharmaceutical research (Subcategory E) does not fall within SIC Codes 2831, 2833, or 2834 (designated to be studied by EPA in the Settlement Agreement) and does not have wastewater characteristics warranting the development of a national regulation. EPA is proposing to limit this exclusion to bench-scale research operations. Therefore, EPA excluded Subcategory E bench-scale research from development of further regulations beyond the 1983 BPT limitations. For the same reasons, Subcategory E bench-scale research is not addressed by these proposed regulations.

EPA has reviewed the additional characterization data collected since the 1983 final rulemaking to determine if the previous subcategorization scheme is still appropriate. The results of that review are described in Section 4.3.

4.3 Proposed Subcategorization Basis

For this rulemaking, EPA is proposing the following four subcategories:

1) Subcategory A - Fermentation Operations;

2) Subcategory B - Biological and Natural Extraction Operations;

3) Subcategory C - Chemical Synthesis Operations; and

4) Subcategory D - Mixing, Compounding, or Formulating Operations.

Where the subcategory operation definitions are as follows:

- Fermentation. A chemical change induced by a living organism or enzyme, specifically, bacteria, or the microorganisms occurring in unicellular plants such as yeast, molds, or fungi. Process operations that utilize fermentation to manufacture pharmaceutically active ingredients define Subcategory A.

- Biological and Natural Extraction. The chemical and physical extraction of pharmaceutically active ingredients from natural sources such as plant roots and leaves, animal glands, and parasitic fungi. The process operations involving biological and natural extraction define Subcategory B.

- Chemical Synthesis. The process(es) of using a chemical reaction or a series of chemical reactions to manufacture pharmaceutically active ingredients. The chemical synthesis process operations define Subcategory C.

- Mixing, Compounding, or Formulating. Processes through which pharmaceutically active ingredients are put in dosage forms. Processes involving mixing, compounding, or formulating define Subcategory D.

This subcategorization scheme is consistent with the conclusions drawn during the subcategorization analysis for the 1983 final rulemaking and with characterization data collected since 1983 and industry profile information gathered with the Detailed Questionnaire.

The following paragraphs discuss EPA's consideration of the nine factors listed in the beginning of this section in determining appropriate subcategories for the pharmaceutical manufacturing industry. The primary bases for subcategorization of facilities in this industry were found to be manufacturing processes and wastewater characteristics.

4.3.1 Manufacturing Processes

There are four basic manufacturing operations used in the pharmaceutical manufacturing industry: 1) fermentation, 2) biological or natural extraction, 3) chemical synthesis, and 4) mixing, compounding, and formulating. The following paragraphs present a brief overview of each of the manufacturing operations and the sources and characteristics of wastewater from each. A detailed discussion of these manufacturing operations is provided in Section 3.4.

Fermentation is the usual method for producing antibiotics and steroids. The process involves three basic steps: inoculum and seed preparation, fermentation, and product recovery. Most of the wastewater is generated from the fermentation and product recovery steps. Fermentation is typically a large-scale batch process. Product recovery is accomplished by solvent extraction, direct precipitation, ion exchange, and/or adsorption. Based on responses to the Detailed Questionnaire, the solvents most often used in fermentation operations are acetone, methanol, isopropanol, ethanol, and amyl alcohol. Priority pollutants used in fermentation operations include methylene chloride, toluene, and phenol. Copper and zinc are priority pollutant metals known to be utilized where precipitation is used for product recovery. Due to the food materials contained in spent fermentation broth, fermentation wastewaters are very amenable to biological treatment. Data from responses to the Detailed Questionnaire show that wastewater from fermentation plants is generally characterized by high BOD_5, COD, and TSS concentrations, large flows, and a pH range of approximately 4.0 to 8.0.

In biological and/or natural extraction manufacturing operations, pharmaceutical products are extracted from such natural sources as plant material, animal glands, and parasitic fungi through a series of volume reduction and chemical extraction steps. These operations are usually conducted on a much smaller scale than fermentation or chemical synthesis operations. The principal sources of wastewater from biological and natural extraction operations are spent raw materials (plant or animal tissue residue),

floor and equipment washes, and spent solvents. Solvents used in purification and extraction steps include the priority pollutants methylene chloride, toluene, chloroform, and 1,2 dichloroethane as well as the nonconventional pollutants ethanol, methanol, n-amyl acetate, isopropanol, and acetone. The priority pollutant phenol is used as a disinfecting chemical in this process. Ammonium salts are used for pH control during the extraction process. Data from responses to the Detailed Questionnaire show that wastewater from extraction operations is generally characterized by relatively low BOD_5, COD, and TSS concentrations, low flows, and pH values ranging from approximately 6.0 to 8.0.

Chemical synthesis is the process by which most drug compounds are manufactured. Chemical synthesis is generally a batch process using a conventional batch reaction vessel and involves techniques such as alkylations, carboxylation, esterifications, halogenations, and sulfonations. During chemical synthesis, wastewater is generally produced with each chemical modification that requires filling and emptying of the batch reactors. Primary sources of wastewater from chemical synthesis operations are process wastes (spent solvents, filtrates, and concentrates), floor and equipment washes, pump seal water, wet scrubber wastewater, and spills. A wide variety of priority pollutant and nonconventional chemicals are used as reaction and purification solvents during chemical synthesis. Priority pollutants used during chemical synthesis include several chlorinated alkanes and chlorinated aromatic compounds. The major nonconventional pollutants reported in the Detailed Questionnaire were methanol, acetone, isopropanol, ethyl acetate, ethanol, and the six-member ring compounds xylene, pyridine, and toluene. Wastewater from chemical synthesis operations is generally characterized by relatively high BOD_5, COD, and TSS concentrations, large flows, and a wide pH range.

Mixing, compounding, and formulating plants receive bulk pharmaceutical active ingredients as raw materials and subsequently manufacture final dosage forms for consumer use (tablets, liquids, capsules, ointments, etc.). Mixing, compounding, and formulating operations typically involve few production steps which generate wastewater.

The primary wastewater sources from these operations are floor and equipment wash water, wet scrubbers, and spills. Wastewater from mixing, compounding, and formulating operations normally has low BOD_5, COD, and TSS concentrations, relatively small flows, and pH values ranging from 6.0 to 8.0.

Each type of manufacturing operation in the pharmaceutical manufacturing industry is distinct. Fermentation and chemical synthesis manufacturing operations are typically large-scale batch processes characterized by large flows and relatively high BOD_5, COD, and TSS concentrations. Biological extraction and mixing, compounding, and formulating operations are characterized by low wastewater flows and relatively low BOD_5, COD, and TSS concentrations.

Because of these distinct manufacturing operations and the related wastewater characteristics, the Agency considered manufacturing processes as a basis for subcategorization of this industry.

4.3.2 Wastewater Characteristics and Treatability

As discussed in Section 4.3.1, each type of manufacturing process in the pharmaceutical manufacturing industry is distinct, and wastewaters are generated by differing unit operations and exhibit somewhat different characteristics. This section summarizes discharge flow and wastewater characterization data submitted by the pharmaceutical manufacturing industry in the Detailed Questionnaire.

Tables 4-1 through 4-4 present flow, raw wastewater, and treated effluent characterization data from responses to the Detailed Questionnaire. The tables are arranged by subcategory (A, B, C, and D) and distinguish direct versus indirect dischargers. Because many facilities have operations from more than one subcategory, some data are presented for subcategory groups in the tables. Facilities with any manufacturing operations from Subcategories A or C, even those with manufacturing

operations from Subcategory B and/or D, were included with the A, C, and A + C only facilities because most of the flow and pollutant load at these facilities comes from Subcategory A or C manufacturing operations. Additional discussion of wastewater characterization data is presented in Section 5.0.

Table 4-1 presents discharge flow rate and BOD_5, COD, and TSS concentration averages and ranges in untreated wastewater. The table shows similar BOD_5, COD, and TSS average concentrations between facilities with Subcategory A and C operations and between facilities with Subcategory B and D operations. The table also shows that facilities with manufacturing operations from Subcategories A and/or C exhibit higher relative flows and BOD_5, COD, and TSS concentrations than those facilities with manufacturing operations from Subcategories B and/or D.

Tables 4-2 and 4-3 present low, high, and average priority and nonconventional organic pollutant concentration summary data for untreated wastewater. Organic pollutant data presented are the sums of individual pollutants reported as being present in the Detailed Questionnaire. These data do not indicate significant differences in pollutant concentrations for organics between Subcategory A and/or C wastewaters and Subcategory B and/or D wastewaters.

Table 4-4 presents low, high, and average pollutant concentration data for BOD_5, COD, and TSS in treated effluent from direct dischargers. These data do not represent the performance of any specific treatment technology, but are indicative of current overall treatment performance within the industry. These data indicate that BOD_5, COD, and TSS are generally treated to lower levels at the Subcategory B and/or D facilities. Section 8 discusses in detail performance of specific wastewater treatment technologies in the pharmaceutical manufacturing industry. The data presented in Section 8 for advanced biological treatment systems, an important treatment technology commonly used in the pharmaceutical manufacturing industry, also indicate that Subcategory

B and/or D facilities treat BOD_5, COD, and TSS to lower levels than can be achieved at the facilities with Subcategory A and/or C manufacturing operations.

The treatment performance data presented in Section 8 do not demonstrate any differentiation in treatment performance for priority and nonconventional organic pollutants among facilities with operations in different subcategories.

In summary, the distinctly different manufacturing operations identified in Section 4.2. result in distinctly different influent flow and pollutant concentrations between facilities with manufacturing operations from Subcategories A and/or C and facilities with manufacturing operations from Subcategories B and/or D. Facilities with manufacturing operations from Subcategories B and/or D are able to achieve lower treated effluent concentrations of BOD_5, COD, and TSS than facilities with operations from Subcategories A and/or C, using the same treatment technology.

4.3.3 Product Types

Manufacturing processes under the SIC code system in the pharmaceutical manufacturing industry are divided into the following:

- SIC 2833 Medicinal Chemicals and Botanical Products;
- SIC 2834 Pharmaceutical Preparations; and
- SIC 2836 Biological Products.

Medicinal chemicals and botanical products include three major product areas: fermentation products, chemical synthesis products, and natural extraction products. Fermentation products are primarily antibiotics and steroids. Chemical synthesis products include intermediates used to produce other chemical compounds as well as hundreds of bulk chemical products. Natural extraction products include such items as gland derivatives, animal bile salts and derivatives, and herb and tissue derivatives. Pharmaceutical preparations (formulation products) are formulated from bulk active

ingredients prior to being marketed to the public. Biological products include materials extracted from biological materials such as vaccines, serums and various plasma derivatives.(4)

Because product types are a function of the manufacturing process used, the Agency concludes that the nature of the product manufactured is incorporated into the basis for subcategorization.

4.3.4 Raw Materials

The pharmaceutical manufacturing industry draws upon worldwide sources for the myriad of raw materials it needs to produce medicinal chemicals. Fermentation operations require many new raw materials falling into general chemical classifications such as carbohydrates, carbonates, steep liquors, nitrogen and phosphorus compounds, anti-foam agents and various acids and bases. These chemicals are used as carbon and nutrient sources (1), as foam control additives, and for pH adjustment in fermentation processes. Various solvents, acids, and bases are also required for extraction and purification processes. Hundreds of raw materials are required for the many batch chemical synthesis processes used by the industry. These include organic and inorganic compounds and are used in gas, liquid, and solid forms.(4)

Plant and animal tissues are also used by the pharmaceutical manufacturing industry to produce various biological and natural extraction products. The raw materials used in formulation operations are the products from other manufacturing operations. These include bulk chemicals from fermentation and chemical synthesis operations and such items as biles, blood fractions, salts, and various derivatives from biological and natural extraction operations.(4)

Because such a vast number and wide variety of raw materials are used within the industry, it is not practical to base subcategories directly on the raw materials used. In

addition, the nature of raw materials used by the pharmaceutical manufacturing industry are related to the manufacturing process, and therefore, are indirectly accounted for in the proposed basis for subcategorization.

4.3.5 Plant Size

The Agency has determined that plant size in terms of production has no significant or consistent impact on the effectiveness of treatment technologies or wastewater characteristics and is therefore not considering plant size as a basis for subcategorization.

4.3.6 Plant Age

The age of a pharmaceutical manufacturing plant is an indefinite parameter primarily due to continual upgrading and modernization most facilities have undertaken in order to remain competitive. The cornerstone age (the age of the original facility) was evaluated relative to raw waste load and treated effluent load without apparent relationship. The Agency is therefore not considering plant age as a basis for subcategorization.

4.3.7 Plant Location

The locations of pharmaceutical manufacturing facilities are typically based on a number of factors, including:

- Sources of raw materials;
- Proximity to markets for products;
- Availability of an adequate water supply;
- Cheap energy sources;
- Proximity to proper modes of transportation;
- Reasonably priced labor markets; and
- Tax considerations.

The majority of pharmaceutical manufacturing plants are located in New Jersey, New York, Pennsylvania, and Puerto Rico. Based on a review of available data, plant location does not affect the characteristics or treatability of process wastewater streams. The Agency is therefore not considering geographic location as a basis for subcategorization.

4.3.8 Nonwater Quality Environmental Impacts

Nonwater quality environmental impacts characteristics for the pharmaceutical manufacturing industry include:

- Sludge production;
- Waste solvent generation;
- Air pollution derived from wastewater generation and treatment; and
- Steam and electrical energy consumption due to wastewater treatment.

These factors all relate to the characteristics of the wastewater treated. Because wastewater characteristics are specifically accounted for in the proposed subcategorization approach, the Agency considers all environmental impacts to be adequately addressed by the proposed subcategorization approach.

4.3.9 Treatment Costs and Energy Requirements

The same treatment unit operation, such as steam stripping to remove volatile organic pollutants, could be utilized to treat wastewater from a variety of sources. However, the cost of treatment and the energy required will vary depending on flow rates and wastewater characteristics. Because wastewater characteristics are specifically accounted

for in the proposed subcategorization approach, treatment costs are adequately addressed. Therefore, while treatment costs, as discussed in Section 10, were considered by the Agency in selecting the technology bases for this proposed regulation, the Agency concludes that subcategorization based on treatment costs is not appropriate.

4.4 Conclusions

Based on EPA's review of industry data, as described earlier in this section, the Agency concludes that it is appropriate to maintain the four existing subcategories based on the different manufacturing operations used by the pharmaceutical manufacturing industry. The four subcategories for the pharmaceutical manufacturing industry are:

- Subcategory A - Fermentation Operations;
- Subcategory B - Biological and Natural Extraction Operations;
- Subcategory C - Chemical Synthesis Operations; and
- Subcategory D - Mixing, Compounding, or Formulating Operations.

Due to the similarities identified above between the characteristics and treatability of wastewater from fermentation and chemical synthesis operations, the Agency is proposing to establish equivalent effluent limitations guidelines for Subcategories A and C. The Agency is also proposing to establish equivalent effluent limitations guidelines for Subcategories B and D due to the similarity in characteristics and treatability of wastewater from biological extraction and mixing, compounding, and formulating operations.

At facilities that conduct fermentation and/or chemical synthesis operations, as well as biological extraction and/or mixing, compounding, or formulating operations, the vast majority of the wastewater discharge flow and pollutant load originates from the fermentation and chemical synthesis operations. Most facilities with fermentation and/or chemical synthesis operations conduct such operations at integrated facilities where other pharmaceutical manufacturing operations are also conducted, with discharges to a

common wastewater treatment system. The Agency's treatment performance data reflect the integrated nature of such facilities.

For the purpose of analyzing and presenting data in subsequent sections of this development document, pharmaceutical manufacturing facilities are considered either Subcategory A and C facilities, or Subcategory B and D facilities. Due to the predominance of wastewater discharge flow and pollutant load from Subcategory A and C operations when these operations are conducted along with other pharmaceutical manufacturing operations at the same facility, and because of the integrated nature of such facilities, facilities with any Subcategory A or C operations are considered Subcategory A and C facilities. Subcategory B and D facilities are those facilities that have Subcategory B and/or D operations only.

Table 4-1

Summary of Discharge Flow Rate, Conventional Pollutants and COD Concentrations in Untreated Wastewater

Type of Discharge	1983 Subcategory	Pollutant	Untreated Wastewater Concentrations (mg/L)			Flow (1,000 gal/day)		
			Low	High	Ave.	Low	High	Ave.
Direct	A only	BOD_5	3,360	5,600	4,480	493	1,250	872
		COD	9,100	10,900	10,000	493	1,250	872
		TSS	264	2,490	1,380	493	1,250	872
	C only	BOD_5	0	812	218	<1	344	142
		COD	0	1,890	718	<1	344	142
		TSS	0	131	55	<1	344	142
	A and C only	BOD_5	22	2,620	975	202	73,300	21,000
		COD	216	5,280	2,410	202	73,300	21,000
		TSS	39	849	332	202	73,300	21,000
	A and/or C + Other(a)	BOD_5	11	9,700	2,230	51	2,000	1,010
		COD	123	16,500	4,050	51	2,000	1,010
		TSS	40	383	185	51	2,000	1,010
Indirect	A only	BOD_5	NA	NA	2,700	47	786	424
		COD	NA	NA	NA	47	786	424
		TSS	NA	NA	757	47	786	424
	C only	BOD_5	1,250	5,430	3,470	<1	1,620	169
		COD	1,200	22,200	7,980	<1	1,620	169
		TSS	19	1,000	265	<1	1,620	169
	A and C only	BOD_5	0	1,770	885	16	2,540	1,280
		COD	0	4,390	2,190	16	2,540	1,280
		TSS	0	888	444	16	2,540	1,280
	A and/or C + Other(a)	BOD_5	95	11,500	2,540	<1	7,310	494
		COD	152	19,700	4,750	<1	7,310	494
		TSS	14	6,070	820	<1	7,310	494

Table 4-1

(Continued)

Type of Discharge	1983 Subcategory	Pollutant	Untreated Wastewater Concentrations (mg/L)			Flow (1,000 gal/day)		
			Low	High	Ave.	Low	High	Ave.
Direct	B only	BOD_5	-	-	-	-	-	-
		COD	-	-	-	-	-	-
		TSS	-	-	-	-	-	-
	D only	BOD_5	0	328	117	2	692	110
		COD	0	1,140	271	2	692	110
		TSS	2	306	63	2	692	110
	BD only	BOD_5	NA	NA	53	NA	NA	63
		COD	NA	NA	27	NA	NA	63
		TSS	NA	NA	16	NA	NA	63
Indirect	B only	BOD_5	1,850	2,350	2,100	2	165	28
		COD	59	3,110	1,240	2	165	28
		TSS	81	552	250	2	165	28
	D only	BOD_5	0	4,650	601	<1	42,600	680
		COD	0	6,610	907	<1	42,600	680
		TSS	0	2,060	283	<1	42,600	680
	BD only	BOD_5	150	2,940	799	1	1,050	186
		COD	184	2,600	1,060	1	1,050	186
		TSS	24	743	265	1	1,050	186

(a)Facilities with combinations of manufacturing operations from other than Subcategories A, B, C, D, AC, and BD are included as other.

NA = Not available.

Table 4-2

Summary of Priority Pollutant Concentrations in Untreated Wastewater

Type of Discharge	Current Subcategory	Cyanide or Priority	# of Facilities Contributing Data	Untreated Wastewater Conc. (mg/L)		
				Low	High	Ave.
Direct	A only	C P	0 0			
	C only	C P	1 4	- 0.4	- 404	4,850 196
	A and C only	C P	1 4	- 20	- 657	1,730 306
	Other(a)	C P	1 6	- 0.3	- 11,900	38 2,860
Indirect	A only	C P	0 0			
	C only	C P	1 17	- 0.2	- 4,850	5 589
	A and C only	C P	0 1	 -	 -	 619
	Other(a)	C P	2 32	229 0	850 79,900	539 3,630
Direct	B only	P	0			
	D only	P	3	0.2	30	10
	B and D only	P	0			
Indirect	B only	P	1	-	-	691
	D only	P	23	0.00	31,400	1,450
	B and D only	P	2	14.65	350	182

(a)"Other subcategory" denotes facilities which manufacture products in the following subcategories or subcategory combinations: ABD, ACD, AD, CD, ABCD, AB, BC, ABC, and BCD.
P - Priority organic pollutants.
C - Cyanide.
B/D facilities did not report any cyanide in their loads or waste streams.

Table 4-3

Summary of Nonconventional Pollutant Concentrations in Untreated Wastewater

Type of Discharge	1983 Subcategory	Ammonia or Other Nonconventionals	# of Facilities Contributing Data	Untreated Wastewater Concentrations (mg/L)		
				Low	High	Ave.
Direct	A only	N A	0 0			
	C only	N A	5 1	16 -	15,600 -	3,270 228
	A and C only	N A	4 1	282 -	7,450 -	3,030 21
	A and/or C + Other(a)	N A	8 5	114 0.05	39,500 842	9,930 332
Indirect	A only	N A	2 1	54 -	107 -	81 0.05
	C only	N A	21 12	0 10	54,100 948	7,530 354
	A and C only	N A	2 0	6,860	20,800	13,900
	A and/or C + Other(a)	N A	52 27	0 0	385,400 217,700	12,900 8,890
Direct	B only	N A	0 0			
	D only	N A	7 1	0 -	14,200 -	3,130 0.7
	B and D only	N A	1 0	-	-	6
Indirect	B only	N A	7 1	0 -	2,010 -	694 16
	D only	N A	54 4	0 0.5	492,400 348	12,900 99
	B and D only	N A	9 0	45 -	49,700	9,200

(a)Facilities with combinations of manufacturing operations from other than Subcategories A, B, C, D, AC, and BD are included as other.

Table 4-4

Summary of Conventional Pollutants and COD Treated Effluent Concentrations

Type of Discharge	1983 Subcategory	Pollutant	Effluent Concentrations (mg/L)		
			Low	High	Ave.
Direct	A only	BOD_5	66	189	128
		COD	1,400	1,700	1,550
		TSS	97	264	180
	C only	BOD_5	0	15	8
		COD	0	923	268
		TSS	0	53	33
	A and C only	BOD_5	8	211	90
		COD	216	834	530
		TSS	9	232	122
	A and/or C + Other(a)	BOD_5	8	68	35
		COD	123	679	277
		TSS	12	143	71
Direct	B only	BOD_5	-	-	-
		COD	-	-	-
		TSS	-	-	-
	D only	BOD_5	0	145	17
		COD	0	1,140	123
		TSS	2	34	11
	B and D only	BOD_5	NA	NA	4
		COD	NA	NA	27
		TSS	NA	NA	16

(a)Facilities with combinations of manufacturing operations from other than Subcategories A, B, C, D, AC, and BD are included as other.

NA = Not available.

REFERENCES

1. U.S. EPA. Pharmaceutical Manufacturing Point Source Category; Interim Final Rulemaking, 41 Federal Register 50676 (November 17, 1976).

2. U.S. EPA. Pharmaceutical Manufacturing Point Source Category Effluent Limitations Guidelines, Pretreatment Standards, and New Source Performance Standards; Proposed Regulation, 47 Federal Register 53584 (November 26, 1982).

3. U.S. EPA, Office of Water. Development Document for Effluent Limitations Guidelines and Standards for the Pharmaceutical Manufacturing Point Source Category. EPA 440/1-83/084, U.S. Environmental Protection Agency, Washington, D.C., September 1983.

4. U.S. EPA, Office of Water. Development Document for Interim Final Effluent Limitations and Proposed New Source Performance Standards for the Pharmaceutical Manufacturing Point Source Category. EPA 440/1-75/060, U.S. Environmental Protection Agency, Washington, D.C., December 1976.

SECTION 5

WATER USE AND WASTEWATER CHARACTERIZATION

5.1 Introduction

The 1990 Detailed Questionnaire and the 1989 Pharmaceutical Screener Questionnaire distributed by EPA identified 304 facilities which used solvents and discharged wastewater from pharmaceutical manufacturing processes. The following information, based on questionnaire and screener responses, is presented in this section:

- Section 5.2 discusses water use and sources of wastewater;
- Section 5.3 discusses wastewater volume by type of discharge;
- Section 5.4 presents water conservation measures;
- Section 5.5 discusses sources of wastewater characterization data; and
- Section 5.6 discusses wastewater characterization.

5.2 Water Use and Sources of Wastewater

As described in Section 3.4.1, there are four types of pharmaceutical manufacturing operations: fermentation; biological and natural extraction; chemical synthesis; and mixing, compounding, or formulating. Water use and sources of wastewater for each process are described in more detail below.

5.2.1 Pharmaceutical Process Wastewater Sources

Process wastewater is defined by 40 CFR 122.2 as "any water which, during manufacturing or processing, comes into direct contact with or results from the

production or use of any raw material, intermediate product, finished product, by-product, or waste product."

Water is used and wastewater is generated in pharmaceutical manufacturing processes as follows:

- Water of reaction: water formed during the chemical reaction.
- Process solvent: water used to transport or support the chemicals involved in the reaction process; this water is usually removed from the process through a separation stage, such as centrifugation, decantation, drying, or stripping.
- Process stream washes: water added to the carrier, spent acid, or spent base which has been separated from the reaction mixture, in order to purify the stream by washing away the impurities.
- Product washes: water added to the reaction medium to purify an intermediate or final product by washing away the impurities (this water is subsequently removed through a separation stage); or water used to wash the crude product after it has been removed from the reaction medium.
- Spent Acid/Caustic: spent acid and caustic streams, which may be primarily water, discharged from the process during the separation steps which follow the reaction step in which acid and basic reagents are used to facilitate, catalyze, or participate.
- Condensed steam: steam used as a sterilizing medium and in steam strippers for solvent recovery and wastewater treatment.

Other sources of process wastewater associated with pharmaceutical manufacturing operations include:

- Air pollution control scrubber blowdown: water or acidic or basic compounds used in air emission control scrubbers to control fumes from reaction vessels, storage tanks, incinerators, and other process equipment.

- Equipment and floor washes: water used to clean process equipment during unit shutdowns and floors during general housekeeping or for spill cleanup.

- Pump seal water: direct contact water used to cool packing and lubricate pumps.

Table 5-1 presents the amount of process wastewater generated daily in the pharmaceutical manufacturing industry that contains the organic pollutants of concern in the pharmaceutical manufacturing industry (see Table 6-1). Table 5-2 presents the amount of process wastewater generated daily which does not contain organic pollutants of concern. Pharmaceutical manufacturing wastewater associated directly with the manufacturing process as well as pump seal water and water from equipment washes is considered process wastewater in Tables 5-1 and 5-2. Table 5-3 presents the amount of wastewater generated daily from the air pollution control devices.

5.2.2 Other Facility Wastewater Sources

In addition to process wastewater, other types of wastewater may be generated during pharmaceutical manufacturing. This wastewater may include noncontact cooling water (used in heat exchangers), noncontact ancillary water (boiler blowdown, bottle washing), sanitary wastewater, and wastewater from other sources (stormwater runoff). Tables 5-4 through 5-7 present the amount of wastewater generated from these sources. Table 5-8 presents the total amount of wastewater generated by pharmaceutical manufacturing facilities by subcategory.

5.3 Wastewater Volume by Type of Discharge

This section discusses the types of wastewater discharges which apply to the pharmaceutical manufacturing industry, the discharge status of the pharmaceutical manufacturing facilities, and presents total industry discharge flow rates by type of discharge.

5.3.1 Type of Discharge Definitions

There are three types of discharge which apply to the pharmaceutical manufacturing industry: direct, indirect, and zero discharge. Definitions for these discharge types are listed below.

Direct discharge refers to the discharge of a pollutant or pollutants directly to surface waters of the United States (not to a POTW). Facilities that directly discharge wastewaters do so under the NPDES permit program.

Indirect discharge refers to the discharge of pollutants indirectly to waters of the United States, through POTWs.

Zero discharge refers to facilities that do not discharge their wastewaters to waters of the United States, as a result of: complete reuse of process water, no water use, recycle off site or within the plant in other manufacturing processes, or disposal on or off site that does not result in discharge to waters of the United States (e.g., by incineration, evaporation, or deep-well injection).

5.3.2 Discharge Status of Pharmaceutical Manufacturing Facilities

As discussed in Section 3.2.4, EPA received 244 responses to the Detailed Questionnaire. A breakdown of facility discharge status for facilities that responded to the Detailed Questionnaire and the 60 indirect discharging Subcategory D facilities with solvent use that did not receive a Detailed Questionnaire are presented in the following table. Seven facilities changed discharge status in the time frame between the screener questionnaire and the Detailed Questionnaire. These facilities reported that they discharged wastewater in the screener questionnaire, but they reported zero discharge in the Detailed Questionnaire.

Subcategory	Number of Direct Discharge Facilities	Number of Indirect Discharge Facilities	Number of Facilities That Have Both Direct and Indirect Discharges	Total
A/C	23	88	1	112
B/D	12	171	2	185
Total	35	259	3	297(a)

(a) Seven facilities reported zero discharge in the Detailed Questionnaire.

The flow rate and wastewater characterization data presented in this section are representative of these 297 facilities.

5.3.3 Flow Rates by Type of Discharge

The total amount of process wastewater discharged from pharmaceutical manufacturing processes to waters of the United States in 1990 was approximately 104.2 MGD, compared to 105.5 MGD generated. Eighty-one percent of all process wastewater discharged was discharged directly to a receiving stream while 19% was discharged indirectly. Over 93% of the wastewater discharged in the pharmaceutical manufacturing industry is from facilities with fermentation and chemical synthesis operations. The following table presents the volumes of pharmaceutical process wastewater discharged by subcategory in 1990.

Subcategory	Volume of Process Wastewater Discharged to Surface Water (MGD)	Volume of Process Wastewater Discharged to POTW (MGD)	Total Process Water Discharged (MGD)
A/C	82.78	14.77	97.55
B/D	1.44	5.21	6.65
Total	84.20	19.98	104.20

5.4 Water Conservation Measures

Water conservation measures were implemented with regard to process wastewater by 137 of the 244 respondents to the Detailed Questionnaire. Water conservation measures implemented include: careful monitoring of water use, installation of automatic monitoring and alarm systems on in-plant discharges, implementation of alternative production processes requiring less water, conversion from barometric to surface condensers, reuse of wastewater from other manufacturing processes, reuse of noncontact water as process makeup water, and treatment of contact cooling water to allow reuse. Table 5-9 presents the number of facilities which implemented these water conservation measures.

The following table, based on the responses to the waste minimization section of the Detailed Questionnaire, presents the number of facilities reporting a reduction in wastewater generated (expressed as a range in gal/yr) between 1989 and 1990.

Reduction in Wastewater Quantity (gal/yr)	Number of Facilities
1 - 9,999	7
10,000 - 99,999	7
100,000 - 499,999	9
500,000 - 1,000,000	0
> 1,000,000	3
Total Number of Facilities	26

5.5 Sources of Wastewater Characterization Data

Section 3.2 described the many wastewater data collection efforts undertaken for development of these effluent limitations guidelines and standards. Sources that produced data on raw wastewater characteristics included the Detailed Questionnaire

and EPA sampling at pharmaceutical manufacturing facilities. Results of these data-gathering efforts are described in more detail below.

5.5.1 Data from the Detailed Questionnaire

The Detailed Questionnaire was used to gather raw wastewater information from pharmaceutical manufacturing facilities for conventional, priority, and nonconventional pollutants. These data are presented in Section 5.6.

5.5.2 EPA Pharmaceutical Manufacturers Sampling Program

To expand and augment the wastewater characterization data obtained in previous data-gathering efforts, EPA conducted sampling episodes at 13 pharmaceutical manufacturing facilities between 1986 and 1991. Through this sampling effort, EPA verified the presence of many of the conventional, priority, and nonconventional pollutants that were indicated as known or believed to be present in pharmaceutical manufacturing wastewater based on earlier data-gathering efforts.

The sampling program was designed to characterize the wastewaters from both direct and indirect dischargers. Direct dischargers selected for participation in the sampling program were those that met the following criteria:

- The facility attained better than BPT-level annual average effluent concentrations for BOD_5, COD, and TSS with its biological treatment system, and
- The facility's raw wastewater discharge contained significant amounts of volatile organic pollutants.

Indirect dischargers selected for participation in the sampling program were those that discharged significant levels of volatile organic pollutants in their wastewater and/or operated a wastewater pretreatment facility. Because EPA concentrated its sampling

efforts at facilities with many pollutants and high concentrations of pollutants, the facilities selected were all Subcategory A and C facilities. Section 5.6 presents wastewater characterization data from these sampling episodes.

5.6 Wastewater Characterization

The pharmaceutical manufacturing industry generates process wastewaters containing a variety of pollutants. Most of this process wastewater receives some treatment, either in-plant at the process unit prior to commingling with other facility wastewaters or in an end-of-pipe wastewater treatment system. This section presents wastewater characterization data for pharmaceutical manufacturing facilities. Data from the Detailed Questionnaire are presented in Sections 5.6.1 through 5.6.3 and data from EPA's sampling program are presented in Section 5.6.4. Section 5.6.5 presents a discussion of sulfide and sulfate containing compounds in pharmaceutical wastewaters.

5.6.1 Conventional Pollutants and COD

The two conventional pollutants in pharmaceutical manufacturing wastewater characterized by data from the Detailed Questionnaire are BOD_5 and TSS.

BOD_5, the quantity of oxygen used in the aerobic stabilization of wastewater streams, is the most widely used measure of general organic pollution in wastewater. This analytical determination involves measuring dissolved oxygen used by microorganisms to biodegrade organic matter, and varies with the amount of biodegradable matter that can be assimilated by biological organisms under aerobic conditions. The nature of specific chemicals discharged into wastewater affects the BOD_5 due to the differences in susceptibility of different molecular structures to microbiological degradation. Compounds with lower susceptibility to decomposition by microorganisms or that are toxic to microorganisms tend to exhibit lower BOD_5 values than compounds that biodegrade readily. Consequently, while BOD_5 can provide a gross indication of the

presence of organic pollutants, it is not a good indicator for the presence of specific toxic organic pollutants.

Total solids in wastewater is defined as the residue remaining upon evaporation at just above the boiling point. TSS is the portion of the total solids that can be filtered out of solution using a 1-micron filter. Raw wastewater TSS content is a function of the manufacturing processes, as well as the manner in which fine solids may be removed during a processing step. The total solids are composed of matter which is settleable, in suspension or in solution, and can be organic, inorganic, or a mixture of both. Settleable portions of the suspended solids are usually removed in a primary clarifier. Finer materials are carried through the system, and in the case of an activated sludge system, become enmeshed with the biomass where they are then removed with the sludge during secondary clarification. Some manufacturing facilities may show an increase in TSS in the effluent from the treatment plant. This characteristic is usually associated with biological systems and indicates that secondary clarification may be inefficient in removing secondary solids. Treatment systems that include polishing ponds or lagoons may also exhibit this characteristic due to algae growth.

COD, a nonconventional pollutant, is also characterized in this section because it is generally used with BOD_5 as a ratio to determine the amount of pollutants in the wastewater. COD is a measure of organic material in wastewater that can be oxidized as determined by subjecting the waste to a powerful chemical oxidizing agent (such as potassium dichromate or potassium permanganate) in an acidic medium. Therefore, the COD test can show the presence of organic materials that are not readily susceptible to attack by biological microorganisms. As a result of this difference, COD values are almost invariably higher than BOD_5 values for the same sample. The COD test cannot be substituted directly for the BOD_5 test because the COD/BOD_5 ratio is extremely variable and is dependent on the specific chemical constituents in the wastewater. In addition, the COD test measures refractory organics, which the BOD_5 test does not. A COD/BOD_5 ratio for the wastewater from a single manufacturing facility with a constant

product mix or from a single manufacturing process may be established. This ratio is applicable only to the wastewater from which it was derived and cannot be used to estimate the BOD_5 of another facility's wastewater. It is often established by facility personnel to monitor process and treatment plant performance with a minimum of analytical delay. COD effluent levels remaining after existing BPT level biological treatment of pharmaceutical wastewater are generally higher than the effluent levels from organic chemicals, plastics, and synthetic fibers (OCPSF) and pesticide facilities following what is considered BPT level treatment in these categories.(1)

Information gathered form the 1987 COD study described in Section 3.2.2 indicates that pharmaceutical manufacturing wastewaters contain COD which is comprised of many organic compounds (not all of which could be identified in the study). Aquatic toxicity tests conducted as part of the study showed that the raw waste exhibited very high chronic toxicity with respect to both reproduction and survival of the species tested.

Untreated wastewater and final effluent wastewater characterization of COD, BOD_5, and TSS was obtained from a table in the Detailed Questionnaire requesting 1990 long-term averages (in mg/L) and flow (in GPD). Table 5-10 presents this information by subcategory and type of discharge. Final effluent data represent the characteristics of wastewater sent to a POTW or discharged to surface water, and do not represent any one level or type of treatment.

Untreated wastewater concentrations and final effluent concentrations reported are not paired data. Low and high concentrations for BOD_5, COD, and TSS presented in Table 5-10 represent the range of values reported and are not from a single facility. The average concentration in the table was calculated by adding the concentration data available from each facility and dividing by the number of facilities.

5.6.2 Priority Pollutants

Priority pollutants proposed for regulation (listed in Section 6.5) were reported as used by 93 pharmaceutical manufacturing facilities in their responses to the Detailed Questionnaire. According to the Detailed Questionnaire, the list of priority pollutants used contained both volatile and semivolatile compounds. The priority pollutants used in the greatest quantities are methylene chloride, toluene, and chloroform. Table 5-11 presents untreated wastewater and final effluent wastewater characterization data for these priority pollutants. Concentrations of priority pollutants in untreated wastewater were calculated from pollutant discharge load information and influent flow rates to the wastewater treatment plant. The pollutant load in untreated wastewater was calculated as the sum of the following: air emissions from wastewater prior to discharge, the pollutant load in wastewater discharged to surface water and/or the sewer, and the pollutant load degraded and/or destroyed in the treatment process. Concentrations of priority pollutants in final effluent wastewater were calculated from the pollutant load in wastewater discharged to surface water and/or the sewer and effluent flow rates from the wastewater treatment plant. Final effluent concentrations represent the concentration of priority pollutants in the wastewater sent to a POTW or discharged to surface water, and do not represent any one level or type of treatment.

The total mass of priority pollutants in untreated wastewater and final effluent was divided by the respective flow rate to calculate untreated wastewater and final effluent concentrations at each facility. Low and high concentrations presented in Table 5-11 represent the range of total concentration values from the facilities in the subcategory. Average concentrations were calculated by adding the total mass of priority pollutants from each facility with available data and dividing by the sum of the flows at these facilities. Discharge loads of specific priority pollutants are presented in Section 9.

5.6.3 Nonconventional Pollutants

Nonconventional pollutants proposed for regulation (listed in Section 6.7) were reported as used by 225 pharmaceutical manufacturing facilities in their responses to the Detailed Questionnaire. According to the respondents, the nonconventional pollutants used in the largest quantities are methanol, ethanol, acetone, and isopropanol. Table 5-12 presents untreated wastewater and final effluent wastewater characterization data for these nonconventional pollutants.

The nonconventional pollutant COD is discussed in Section 5.6.1 because COD data were collected in the same manner as BOD_5 and TSS data. In addition, COD/BOD_5 ratios are used by facilities to monitor pharmaceutical manufacturing processes and treatment plant performance.

Ammonia is shown separately in Table 5-12 since it is not an organic compound and has rather distinct characteristics. Analytical data were collected for both ammonia and ammonium hydroxide. However, ammonia is assumed to be in equilibrium with ammonium hydroxide in aqueous solution.(2)

$$NH_3 + H_2O \rightleftarrows NH_4OH \qquad (5\text{-}1)$$

Ammonium hydroxide, in turn, is in equilibrium with ammonium ion and hydroxide ion in aqueous solution.

$$NH_4OH \rightleftarrows NH_4^+ + OH^- \qquad (5\text{-}2)$$

Equilibrium in Equation 5-1 strongly favors ammonia, while equilibrium in Equation 5-2 strongly favors the ions.

In Table 5-12, concentrations of nonconventional pollutants in untreated wastewater were calculated from pollutant discharge load information and influent flow rates to the wastewater treatment plant. The pollutant load in untreated wastewater was calculated as the sum of the following: air emissions from wastewater prior to discharge, the pollutant load in wastewater discharged to surface water and/or the sewer, and the pollutant load degraded and/or destroyed in the treatment process. Concentrations of nonconventional pollutants in final effluent wastewater were calculated from the pollutant load in wastewater discharged to surface water and/or the sewer and effluent flow rates from the wastewater treatment plant. Final effluent concentrations represent the concentration of nonconventional pollutants in the wastewater sent to a POTW or discharged to surface water, and do not represent any one level or type of treatment.

The total mass of nonconventional pollutants in untreated wastewater and final effluent was divided by the respective flow rate to calculate untreated wastewater and final effluent concentrations at each facility. Low and high concentrations presented in Table 5-12 represent the range of concentration values from the facilities in the subcategory. Average concentrations were calculated by adding the total mass of nonconventional pollutants from each facility with available data and dividing by the sum of the flows at these facilities. Discharge loads of specific nonconventional pollutants are presented in Section 9.

5.6.4 Sampling Data

Table 5-13 summarizes untreated wastewater and final effluent wastewater characterization data from EPA sampling episodes. Priority and nonconventional pollutants in the table refer only to pollutants proposed for regulation in Sections 6.6 and 6.7. Untreated wastewater data were collected from 11 of the 13 pharmaceutical facilities sampled. Final effluent data were collected from 8 of the 13 pharmaceutical facilities sampled. Final effluent wastewater characterization data do not represent any

one level or type of treatment. Treatment performance data for specific treatment technologies are presented in Section 8.

Untreated wastewater concentrations and final effluent concentrations reported are not paired data. Low and high concentrations for ammonia, COD, nonconventional organics, and priority organics presented in Table 5-13 represent the range of values reported and are not from a single facility. The priority organic and nonconventional organic concentrations presented are the sum of the concentrations of individual organic constituents detected at the respective facilities. The average concentration was calculated by adding the concentration data available from each facility and dividing by the number of facilities. Full sets of sampling characterization data can be found in the sampling episode reports in the Record for this rulemaking.

5.6.5 Sulfide/Sulfate Containing Compounds

EPA has discussed with representatives of POTWs which receive pharmaceutical manufacturing wastewaters concerns related to sulfide/sulfate containing compounds discharged into POTW sewer systems. Sulfide and sulfate containing compounds discharged to POTW sewers are converted to hydrogen sulfide and released into the air under low pH conditions in the sewer lines or pumping stations leading to the POTW. The hydrogen sulfide that is produced has been measured at concentrations that create a worker safety concern and may also be an explosion concern. EPA is currently soliciting additional information on the occurrence of sulfide and sulfate containing compounds in pharmaceutical wastewaters and the treatment of these compounds to minimize worker safety and explosion concerns. Current treatment approaches that the Agency is aware of to reduce hydrogen sulfide emissions from POTW sewer lines include pH monitoring and the addition of ferrous chloride to sequester the sulfides in wastewater and also the addition of peroxide at pumping stations to oxidize hydrogen sulfide.

Table 5-1

Process Wastewater Generated Which Contains Organic Compounds

Subcategory and Discharge Mode	Average Quantity Generated (MGD)
A and/or C Direct	77.62
A and/or C Indirect	10.54
B and/or D Direct	0.15
B and/or D Indirect	3.12
Total	**91.43**

Table 5-2

Process Wastewater Generated Which Does Not Contain Organic Compounds

Subcategory and Discharge Mode	Average Quantity Generated (MGD)
A and/or C Direct	5.45
A and/or C Indirect	5.03
B and/or D Direct	1.29
B and/or D Indirect	2.31
Total	**14.08**

Table 5-3
Wastewater Resulting From
Air Pollution Control

Subcategory and Discharge Mode	Average Quantity Generated (MGD)
A and/or C Direct	1.85
A and/or C Indirect	2.14
B and/or D Direct	0.01
B and/or D Indirect	0.33
Total	**4.33**

Table 5-4

Wastewater Resulting From
Noncontact Cooling Water

Subcategory and Discharge Mode	Average Quantity Generated (MGD)
A and/or C Direct	55.71
A and/or C Indirect	42.36
B and/or D Direct	10.72
B and/or D Indirect	4.99
Total	**113.78**

Table 5-5

Wastewater Resulting From Noncontact Ancillary Water

Subcategory and Discharge Mode	Average Quantity Generated (MGD)
A and/or C Direct	16.72
A and/or C Indirect	4.24
B and/or D Direct	0.83
B and/or D Indirect	2.24
Total	**24.03**

Table 5-6

Sanitary Wastewater

Subcategory and Discharge Mode	Average Quantity Generated (MGD)
A and/or C Direct	1.10
A and/or C Indirect	4.46
B and/or D Direct	0.77
B and/or D Indirect	2.96
Total	**9.29**

Table 5-7

Wastewater From Other Sources

Subcategory and Discharge Mode	Average Quantity Generated (MGD)
A and/or C Direct	3.22
A and/or C Indirect	2.44
B and/or D Direct	0.48
B and/or D Indirect	3.34
Total	**9.48**

Table 5-8
Total Amount of Wastewater Generated from Pharmaceutical Manufacturing Facilities

Subcategory and Discharge Mode	Total Quantity Generated (MGD)
A and/or C Direct	161.67
A and/or C Indirect	71.21
B and/or D Direct	14.25
B and/or D Indirect	19.29
Total	**266.42**

Table 5-9

Water Conservation Measures Implemented For Process Wastewater(a)

Water Conservation Measure	Implemented Last 5 Years	Implemented Earlier	Total Responses
Careful monitoring of water use	79	58	137
Installation of automatic monitoring and alarm systems on in-plant discharges	36	20	56
Implementation of alternative production processes requiring less water	20	6	26
Conversion from barometric to surface condensers	6	12	18
Reuse of noncontact water as process makeup water	3	6	9
Reuse of wastewater from other manufacturing processes	6	3	9
Treatment of contact cooling water to allow reuse	4	4	8

(a)Of the 244 facilities completing the Detailed Questionnaire, 137 responded that water conservation measures were implemented with regard to process wastewater.

Table 5-10

BOD_5, COD, and TSS Concentrations in Untreated Wastewater and Final Effluent

Type of Discharge	Current Subcategory	Pollutant	Untreated Wastewater Conc. (mg/L)			Final Effluent Conc. (mg/L)			Flow (1,000 GPD)		
			Low	High	Ave.	Low	High	Ave.	Low	High	Ave.
Direct	A only	BOD_5	3,360	5,600	4,480	66	189	128	493	1,250	872
		COD	9,100	10,900	10,000	1,400	1,700	1,550	493	1,250	872
		TSS	264	2,490	1,380	97	264	180	493	1,250	872
	C only	BOD_5	NA	812	218	0	15	8	0	344	142
		COD	NA	1,890	718	0	923	268	0	344	142
		TSS	NA	131	55	0	53	33	0	344	142
	A and C only(a)	BOD_5	22	2,620	975	8	211	90	202	73,300	21,000
		COD	216	5,280	2,410	216	834	530	202	73,300	21,000
		TSS	39	849	332	9	232	122	202	73,300	21,000
	Other(b)	BOD_5	11	9,700	2,230	8	68	35	51	2,000	1,000
		COD	123	16,500	4,050	123	679	277	51	2,000	1,000
		TSS	40	383	185	12	143	71	51	2,000	1,000
Indirect	A only(a)	BOD_5	NA	NA	2,690	300	2,690	1,500	47	786	424
		COD	NA	NA	NA	NA	NA	566	47	786	424
		TSS	NA	NA	757	757	1,560	1,160	47	786	424
	C only(a)	BOD_5	1,250	5,430	3,470	23	5,300	1,090	0	1,620	169
		COD	1,200	22,200	7,980	267	22,200	4,030	0	1,620	169
		TSS	19	1,000	265	14	2,110	254	0	1,620	169
	A and C only(a)	BOD_5	NA	1,770	885	0	1,770	885	16	2,540	1,280
		COD	NA	4,390	2,200	0	4,390	2,200	16	2,540	1,280
		TSS	NA	888	444	0	888	444	16	2,540	1,280
	Other(a,b)	BOD_5	95	11,500	2,540	0	32,800	2,400	0	7,310	494
		COD	152	19,700	4,750	282	19,700	3,030	0	7,310	494
		TSS	14	6,070	820	0	5,810	565	0	7,310	494

Table 5-10

(Continued)

Type of Discharge	Current Subcategory	Pollutant	Untreated Wastewater Conc. (mg/L)			Final Effluent Conc. (mg/L)			Flow (1,000 GPD)		
			Low	High	Ave.	Low	High	Ave.	Low	High	Ave.
Direct	B only	BOD_5	-	-	-	-	-	-	-	-	-
		COD	-	-	-	-	-	-	-	-	-
		TSS	-	-	-	-	-	-	-	-	-
	D only	BOD_5	NA	328	117	0	145	17	2	692	110
		COD	NA	1,140	271	0	1,140	123	2	692	110
		TSS	2	306	63	2	34	11	2	692	110
	B and D only	BOD_5	NA	NA	53	NA	NA	4	NA	NA	63
		COD	NA	NA	27	NA	NA	27	NA	NA	63
		TSS	NA	NA	16	NA	NA	16	NA	NA	63
Indirect	B only(a)	BOD_5	1,850	2,350	2,100	300	2,350	1,500	2	165	28
		COD	59	3,110	1,240	59	4,480	1,740	2	165	28
		TSS	81	552	250	9	552	209	2	165	28
	D only(a)	BOD_5	NA	4,650	601	0	4,950	580	0	42,600	680
		COD	NA	6,610	907	0	2,660	502	0	42,600	680
		TSS	NA	2,060	283	0	2,410	238	0	42,600	680
	B and D only(a)	BOD_5	150	2,940	800	10	307	140	1	1,050	186
		COD	184	2,600	1,070	184	413	282	1	1,050	186
		TSS	24	743	265	24	100	63	1	1,050	186

(a)Some of these facilities provided BOD_5, COD, and TSS loadings and flows by stream. The loadings and flows were summed for all streams in the facility, and the total concentration and flow were used in this average.

(b)"Other Subcategory" denotes facilities which manufacture products in the following subcategories or subcategory combinations: ABD, ACD, AD, CD, ABCD, AB, BC, ABC, and BCD.

NA - Not available.

Table 5-11

Cyanide and Total Priority Organic Pollutant Concentrations in Pharmaceutical Manufacturing Process Wastewater

Type of Discharge	Current Subcategory	Cyanide or Priority	# of Facilities Contributing Data	Untreated Wastewater Conc. (mg/L)			Final Effluent Conc. (mg/L)			Flow (1,000 GPD)		
				Low	High	Ave.	Low	High	Ave.	Low	High	Ave.
Direct	A only	C P	0 0									
	C only	C P	1 4	- 0.4	- 404	4,850 196	- 0	- 5	5 2	- 3	- 1,340	2 389
	A and C only	C P	1 4	- 20	- 657	1,730 306	- 0	- 17	0.4 5	- 114	- 7,210	3 2,160
	Other(a)	C P	1 6	- 0.3	- 11,900	38 2,860	- 0	- 141	0.2 28	- 21	- 1,220	3 379
Indirect	A only	C P	0 0									
	C only	C P	1 17	- 0.2	- 4,850	5 589	- 0	- 1,280	0.4 94	- 0	- 862	1 121
	A and C only	C P	0 1	-	-	619	-	-	61	-	-	154
	Other(a)	C P	2 32	229 0	850 79,900	539 3,630	0 0	1 79,900	0.5 2,670	0 0	30 1,010	15 201
Direct	B only	P	0									
	D only	P	3	0.2	30	10	0	0	0	11	34	21
	B and D only	P	0									

Table 5-11

(Continued)

Type of Discharge	Current Subcategory	Cyanide or Priority	# of Facilities Contributing Data	Untreated Wastewater Conc. (mg/L)			Final Effluent Conc. (mg/L)			Flow (1,000 GPD)		
				Low	High	Ave.	Low	High	Ave.	Low	High	Ave.
Indirect	B only	P	1	-	-	691	-	-	0	-	-	11
	D only	P	23	0.00	31,400	1,450	0	31,400	1,380	0	278	28
	B and D only	P	2	14.65	350	182	2	15	8	13	676	345

(a)"Other subcategory" denotes facilities which manufacture products in the following subcategories or subcategory combinations: ABD, ACD, AD, CD, ABCD, AB, BC, ABC, and BCD.
P - Priority organic pollutants.
C - Cyanide.
B and D facilities did not report any cyanide in their loads or waste streams.

Table 5-12

Ammonia and Total Nonconventional Organic Pollutant Concentrations in Pharmaceutical Manufacturing Process Wastewater

Type of Discharge	Current Subcategory	Ammonia or Nonconventional	# of Facilities Contributing Data	Untreated Wastewater Conc. (mg/L)			Final Effluent Conc. (mg/L)			Flow (1,000 GPD)		
				Low	High	Ave.	Low	High	Ave.	Low	High	Ave.
Direct	A only	N A	0 0									
	C only	N A	5 1	16 -	15,600 -	3,270 228	0.3 -	155 -	36 39	3 -	1,340 -	322 1,340
	A and C only	N A	4 1	282 -	7,450 -	3,030 21	0 -	138 -	35 19	114 -	7,210 -	2,160 7,210
	Other(a)	N A	8 5	114 0.05	39,500 842	9,930 332	0 0	432 600	110 151	21 21	1,220 720	298 224
Indirect	A only	N A	2 1	54 -	107 -	81 0.05	54 -	107 -	81 0.05	24 -	800 -	412 24
	C only	N A	21 12	0 10	54,100 948	7,530 354	0 0	20,800 875	2,760 116	0 0	862 862	99 153
	A and C only	N A	2 0	6,860	20,800	13,900	1,720	20,800	11,300	0	154	77
	Other(a)	N A	52 27	0 0	385,000 218,000	12,900 8,890	0 0	366,000 11,600	10,200 450	0 0	1,010 987	134 187
Direct	B only	N A	0 0									
	D only	N A	7 1	0 -	14,300 -	3,130 0.7	0 -	6,110 -	928 0	0 -	20 -	6 13
	B and D only	N A	1 0	-	-	6	-	-	6	-	-	63

Table 5-12

(Continued)

Type of Discharge	Current Subcategory	Ammonia or Nonconventional	# of Facilities Contributing Data	Untreated Wastewater Conc. (mg/L)			Final Effluent Conc. (mg/L)			Flow (1,000 GPD)		
				Low	High	Ave.	Low	High	Ave.	Low	High	Ave.
Indirect	B only	N	7	0	2,010	694	0	1,700	423	0	200	32
		A	1	-	-	16	-	-	0	-	-	1
	D only	N	54	0	492,000	12,900	0	492,000	10,600	0	309	23
		A	4	0.5	348	99	0	44	12	0	5	2
	B and D only	N	9	45	49,700	9,200	45	48,400	6,840	0	676	101
		A	0	-								

(a)"Other subcategory" denotes facilities which manufacture products in the following subcategories or subcategory combinations: ABD, ACD, AD, CD, ABCD, AB, BC, ABC, and BCD.
A - Ammonia.
N - Nonconventional organic pollutants.

Table 5-13

Pharmaceutical Manufacturing Industry Wastewater Characterization Data Based on EPA Sampling Episodes

Type of Discharge	Sub-category	Pollutant	# of Data Points	Untreated Wastewater Conc. (mg/L)			Flow (1,000 GPD)			# of Data Points	Final Effluent Conc. (mg/L)			Flow (1,000 GPD)		
				Low	High	Ave.	Low	High	Ave.		Low	High	Ave.	Low	High	Ave.
Direct	C only	ammonia	2	170	220	195	1,830	1,960	1,900	2	120	130	125	1,830	1,960	1,900
		COD	3	2,200	4,100	2,870	1,830	2,120	1,970	2	380	400	390	1,830	1,960	1,900
		Total non-conventional organics	3	18	190	104	1,960	2,120	2,070	2	0.1	0.2	0.1	1,830	1,960	1,900
		Total priority organics	6	1	12	6	1,830	2,120	2,050	3	0.04	0.2	0.1	1,830	1,960	1,920
	A and C only	ammonia	20	0.5	100	24	950	32,500	4,450	24	0.5	160	58	950	50,000	12,000
		COD	17	63	10,000	3,940	950	32,500	4,320	18	63	2,200	567	950	50,000	6,850
		Total non-conventional organics	53	0.1	236	48	950	32,500	2,560	34	0.1	8	1	1,100	50,000	12,000
		Total priority organics	70	0.08	1,440	207	950	32,500	2,210	48	0.06	4	1	950	50,000	6,430
	Other(a)	ammonia	6	23	49	42	920	1,120	1,030	10	1	4	3	860	1,090	1,020
		COD	6	4,800	6,500	5,450	920	1,120	1,030	11	400	550	482	860	1,210	1,040
		Total non-conventional organics	86	1,530	2,980	2,140	920	1,120	1,060	47	15	101	26	860	1,210	1,060
		Total priority organics	42	6	11	8	920	1,120	1,030	2	0.1	0.1	0.1	990	990	990

Table 5-13

(Continued)

Type of Discharge	Sub-category	Pollutant	# of Data Points	Untreated Wastewater Conc. (mg/L)			Flow (1,000 GPD)			# of Data Points	Final Effluent Conc. (mg/L)			Flow (1,000 GPD)		
				Low	High	Ave.	Low	High	Ave.		Low	High	Ave.	Low	High	Ave.
Indirect	A and C only	ammonia	2	26	35	31	1,860	1,860	1,860	0	NA	NA	NA	NA	NA	NA
		COD	2	9,700	10,000	9,850	1,860	1,860	1,860	0	NA	NA	NA	NA	NA	NA
		Total non-conventional organics	2	1	2	2	1,860	1,860	1,860	0	NA	NA	NA	NA	NA	NA
		Total priority organics	4	0.06	0.6	0.4	1,860	1,860	1,860	0	NA	NA	NA	NA	NA	NA
	Other(a)	ammonia	7	6	81	37	160	2,950	1,510	6	55	190	102	700	1,930	972
		COD	11	1,600	14,000	7,230	80	2,950	1,160	7	800	12,000	4,380	700	2,120	1,140
		Total non-conventional organics	22	2	1,910	412	80	2,950	1,310	9	0.1	2,160	691	700	2,120	1,360
		Total priority organics	24	8	312	62	80	2,950	1,410	13	0.2	13	5	700	2,120	1,470

(a)"Other subcategory" denotes facilities which manufacture products in the following subcategories or subcategory combinations: ABD, ACD, AD, CD, ABCD, AB, BC, ABC, and BCD.
NA - Not available.

REFERENCES

1. Memorandum: The COD of Pharmaceutical Wastewaters, from Frank Hund to the Public Record. April 1, 1988.

2. Memorandum from Alan Messing, DynCorp-Viar. April 4, 1994.

SECTION 6

POLLUTANTS SELECTED FOR REGULATION

6.1 Introduction

EPA has reviewed wastewater characterization data available from the Detailed Questionnaire responses and EPA sampling results to determine the presence or absence of conventional, nonconventional, and priority pollutants in pharmaceutical manufacturing process wastewaters. Using this information, EPA determined pollutants likely to be present and pollutants identified as being discharged by the pharmaceutical manufacturing industry. This section presents the results of that study and identifies the pollutants and pollutant parameters the Agency proposes to regulate under BPT, BCT, and BAT effluent limitations guidelines and NSPS, PSNS, and PSES, as appropriate.

EPA is authorized to regulate conventional and priority pollutants under Sections 304(a)(4) and 301(b)(2)(C) of the Clean Water Act (CWA), respectively. The list of toxic pollutants from Section 307 of the CWA has been expanded to include 126 priority pollutants identified in the Settlement Agreement of NRDC vs. Train.(1) In addition, the Agency may also regulate other nonconventional pollutants, taking into account factors such as treatable amounts, toxicity, analytical methods, frequency of occurrence, use of indicator pollutants, and the pass through of pollutants at Publicly Owned Treatment Works (POTWs).

The following information is discussed in these sections:

- Section 6.2 discusses the pollutants considered for regulation;
- Section 6.3 discusses the pollutants discharged by the pharmaceutical manufacturing industry;

- Section 6.4 presents the pollutant selection evaluation criteria;
- Section 6.5 discusses the conventional pollutants selected for regulation;
- Section 6.6 discusses the priority pollutants selected for regulation; and
- Section 6.7 discusses the nonconventional pollutants selected for regulation.

6.2 Pollutants Considered for Regulation

Prior to 1986, the Agency's regulatory focus for the pharmaceutical manufacturing industry was on five conventional pollutants and 126 priority pollutants. In 1986, the Agency expanded the analysis of the industry's wastewater to determine the presence and levels of the Industrial Technology Division (ITD) List of Analytes, which was derived from the ITD List of Lists, as described in Section 3.2.3. The List of Analytes was revised in 1990 to include 458 analytes. EPA conducted a study to determine which of these 458 analytes could potentially be discharged in pharmaceutical manufacturing wastewaters in significant amounts. The study included a review of the prior pharmaceutical rulemaking and available literature, an evaluation of EPA and industry sampling data obtained prior to 1986, data reported in the Detailed Questionnaire, data submitted by the industry in connection with the Detailed Questionnaire, and data obtained from EPA sampling at pharmaceutical manufacturing facilities.(2) These data-collection efforts are discussed in greater detail in Section 3.

The Agency's evaluation of the industry resulted in a list of 146 conventional, nonconventional, and priority pollutants and pollutant parameters which may be present in the industry's wastewater (see Table 6-1). The pollutants and pollutant parameters identified as likely to be present are predominantly volatile and semivolatile organic compounds. Other parameters which may be present are ammonia and cyanide. Although metals are used in some pharmaceutical manufacturing processes, they were

not discharged at concentrations high enough to warrant control on an industry-wide basis. Section 3 describes in detail the criteria used by the Agency to identify those pollutants which may be present in the industry's wastewater.

6.3 Pollutants Discharged by the Pharmaceutical Industry

EPA requested discharge information on 143 of the 146 pollutants and pollutant parameters which may be present in the industry's wastewater in the Detailed Questionnaire sent to pharmaceutical manufacturing facilities in Subcategories A, B, C, and D. Discharge information was not collected on pH, oil and grease, and fecal coliform. Regulations on governing control of pH in Pharmaceutical Manufacturing wastewater are not being revised. Oil and grease and fecal coliform are not significant pollutants in this industry. The Agency used the responses to this questionnaire to identify which of the pollutants likely to be present were being discharged by the industry.

Responses to Section 3-1 of the Detailed Questionnaire indicated that the following 16 priority pollutants and 35 nonconventional pollutants identified as potentially present in the industry's wastewater were not reported as discharged in pharmaceutical manufacturing wastewaters or air emissions from wastewaters in 1990:

Priority Pollutants Not Reported as Discharged	
Acrolein	1,2-Dichloropropane
Benzidine	Hexachlorocyclapentadiene
Bromoform	Hexachloroethane
Bromomethane	Nitrobenzene
Chloroethane	2-Nitrophenol
p-Dichlorobenzene	4-Nitrophenol
1,1-Dichloroethane	Trichloroethylene
1,1-Dichloroethene	Vinyl Chloride

Nonconventional Pollutants Not Reported as Discharged	
Acetophenone	Epichlorohydrin
4-Aminobiphenyl	Ethyl Cyanide
Benzotrichloride	2-Hexanone
Benzyl Bromide	Iodoethane
Biphenyl	2-Methoxyaniline
2-Bromo-Propanoylbromide	Methyl Methacrylate
sec-Butyl Alcohol	N-Nitrosomorpholine
Catechol	n-Pentane
2-Chloroacetophenone	B-Propiolactone
3-Chloro-4-Fluoroaniline	1,3-Propane Sulfone
Chloromethyl Methyl Ether	Propionaldehyde
Cresol (Mixed)	1,2-Propyleneimine
Cumene	Styrene
1,2-Dibromoethane	Tetrachloroethene
Diethyl Carbonate	1,2-trans-Dichloroethene
Diethyl-ortho Formate	2,4,5-Trichlorophenol
1,1-Dimethylhydrazine	Vinyl Acetate
N-Dipropylamine	

These 16 priority and 35 nonconventional pollutants were excluded from consideration for regulation, leaving 92 conventional, priority, and nonconventional pollutants and pollutant parameters reported as discharged as potential candidates for regulation.

6.4 Pollutant Selection Evaluation Criteria

Having identified those pollutants of concern being discharged by the pharmaceutical manufacturing industry, the Agency next considered which of those pollutants should be controlled. The NRDC Consent Decree included a defined set of criteria for selecting pollutant parameters to be regulated.(1) While no longer bound by the conditions of the NRDC Consent Decree, the Agency used a similar screening protocol for selecting

pollutants and pollutant parameters for this proposed regulation. Pollutants were excluded from consideration for regulation based on the following criteria:

- The pollutant is discharged in relatively small amounts (<3,000 lbs per year, which is ≤ 0.05% of the total pollutant mass discharge), and is neither causing nor likely to cause toxic effects;
- The pollutant is effectively treated by treatment technologies in place;
- The pollutant is reported or detected in the effluent from a small number of sources; and/or
- The pollutant cannot be analyzed by EPA-approved or other state-of-the-art established methods.

The Agency considered the available pollutant data (from existing rulemakings and available literature, evaluation of existing data, data obtained from the Detailed Questionnaire, data submitted by industry, and data obtained from EPA sampling at pharmaceutical manufacturing facilities) against the selection criteria cited above. Sections 6.4.1 through 6.4.5 summarize EPA's assessment of these evaluation criteria for 88 priority and nonconventional pollutants discharged by the pharmaceutical manufacturing industry. The other 4 of the 92 constituents identified as being discharged by the pharmaceutical manufacturing industry (cyanide, COD, and the conventional pollutants BOD_5 and TSS) are considered in Sections 6.5, 6.6, and 6.7. Table 6-2 summarizes the information obtained for each of the 88 priority and nonconventional pollutants identified as discharged by the pharmaceutical manufacturing industry.

6.4.1 Quantity Discharged

The quantity of each of the 88 priority and nonconventional pollutants discharged by the pharmaceutical manufacturing industry in 1990 ranged from 1 lb/yr to 15,400,000 lbs/yr. Table 6-2 lists these pollutants by total quantity discharged in process wastewaters and

air emissions from process wastewaters. Table 6-2 also presents the percentage of total organic loading contributed by each constituent. Those pollutants discharged at 121,000 lbs/yr and above represent approximately 99% of the total organic loading discharged in 1990.

6.4.2 Toxicity

The Agency developed a hazard ranking score for each pollutant based on values relating to the pollutant's freshwater acute toxicity, human health toxicity, oral mammalian toxicity, bioconcentration potential, and persistence in water (based on the pollutant's volatility).(3)

The hazard scores for the 88 pollutants on Table 6-2 and ammonia range from -5 to 22 (the higher the score, the greater the hazard). The highest hazard score possible for a constituent is 49. The hazard scores are on a relative scale, and do not represent absolute rankings.

6.4.3 Treatability

Pollutant treatability was evaluated for the two main technologies utilized by the pharmaceutical manufacturing industry, biological treatment and distillation/steam stripping. Distillation/steam stripping treatability was evaluated using a pollutant's Henry's Law Constant. Biological treatability was evaluated by considering available biotreatability rate constants (Kmax) and/or the ratio of BOD to theoretical oxygen demand (ThOD) (4,5). Henry's Law and Kmax constants, as well as the BOD/ThOD ratio, are general indicators of treatability. All pollutants were found to be treatable by either steam stripping or biological treatment.

6.4.4 Number of Facilities Discharging Pollutants

Table 6-2 lists the number of facilities reporting discharges of each pollutant.

6.4.5 Analytical Methods

Table 6-2 also presents the type of EPA-approved or established state-of-the-art analytical methods available for analysis of each pollutant. Section 18 provides specific information pertaining to the analytical methods proposed for each of the pollutants discharged by the industry.

6.5 Conventional Pollutants Selected for Regulation

Conventional pollutants include BOD_5, TSS, fecal coliform, pH, and oil and grease. These pollutants are general indicators of water quality rather than specific compounds. BOD_5, TSS, and pH are regulated by current BPT limitations; EPA is proposing to revise the BPT limitations for BOD_5 and TSS and to retain the existing BPT limitations for pH.

Oil and grease and fecal coliform were not considered for regulation in the pharmaceutical manufacturing industry. Although oil and grease may appear in some plant process wastewater, it is not sufficiently widespread or discharged at concentrations high enough to justify regulation on an industry-wide basis. Fecal coliform is related to sanitary discharges and not discharges from specific pharmaceutical manufacturing process wastewaters and, therefore, was also not considered for regulation.

6.6 Priority Pollutants Selected for Regulation

Thirty-two priority pollutants were considered for regulation in the pharmaceutical manufacturing industry (see Table 6-1). Sixteen of these were not reported as discharged in pharmaceutical manufacturing wastewaters or air emissions from wastewaters based

on the Detailed Questionnaire. Of the remaining 16 priority pollutants which were discharged, the following 10 were identified as candidates for regulation:

Benzene
Chlorobenzene
Chloroform
Chloromethane (Methyl chloride)
Cyanide
o-Dichlorobenzene (1,2-Dichlorobenzene)
1,2-Dichloroethane
Methylene chloride
Phenol
Toluene

The Agency has previously regulated cyanide in the pharmaceutical manufacturing industry under BPT and is proposing to revise those regulations.

The remaining six priority pollutants considered were not selected for regulation because they were discharged on an industry-wide basis at less than 3,000 lbs/yr. A review of their toxicity, treatability, treatment performance data availability, number of facilities discharging, analytical methods, and load discharged does not support the need for regulation. Table 6-3 lists these six priority pollutants and the reasons for their exclusion from the list of pollutants to regulate.

6.7 Nonconventional Pollutants Selected for Regulation

One hundred and nine nonconventional pollutants were considered for regulation in the pharmaceutical manufacturing industry (see Table 6-1). Thirty-five of these were not reported as discharged in pharmaceutical manufacturing wastewaters or air emissions from process wastewaters based on the Detailed Questionnaire. Of the remaining 74 nonconventional pollutants which were discharged, the following 46 have been identified by the Agency as candidates for regulation:

Acetone
Acetonitrile
Ammonia
n-Amyl acetate
Amyl alcohol
Aniline
2-Butanone (MEK)
n-Butyl acetate
n-Butyl alcohol
tert-Butyl alcohol
COD (Chemical Oxygen Demand)
Cyclohexane
Diethylamine
N,N-Dimethylacetamide
Dimethylamine
N,N-Diemethylaniline
Diethyl ether
N,N-Dimethylformamide
Dimethyl sulfoxide
1,4-Dioxane
Ethanol
Ethyl acetate
Ethylene glycol
Formaldehyde
Formamide
Furfural
n-Heptane
n-Hexane
Isobutyraldehyde
Isopropanol
Isopropyl acetate
Isopropyl ether
Methanol
Methylamine
Methyl cellosolve
Methyl formate
2-Methyl pyridine
Methyl isobutyl ketone (MIBK)
Petroleum naphtha
Polyethylene glycol 600
n-Propanol
Pyridine
Tetrahydrofuran
Trichlorofluoromethane
Triethylamine
Xylenes

The remaining 28 nonconventional pollutants considered were not selected for regulation for the following reasons:

- Twenty-three pollutants were discharged on an industry-wide basis at less than 3,000 lbs/yr. A review of their toxicity, treatability, treatment performance data availability, number of facilities discharging, analytical methods, and load discharged does not support the need for regulation.

- Acetic acid and formic acid were excluded due to their low toxicity and because they will be treated by normal pH control measures as required by the pH range specified within the regulation.

- Glycol ethers were excluded due to the lack of an available analytical method. Methyl cellosolve, the predominant glycol ether

reported as being used by the industry, has been selected for regulation.

- Dimethyl carbamyl chloride and Bis(chloromethyl)ether were excluded because they hydrolize in water and therefore do not persist in water. Formaldehyde, a hydrolysis product of Bis (chloromethyl) ether, is being selected for regulation.

Table 6-4 lists these 28 nonconventional pollutants and the reasons for their exclusion from the list of pollutants to regulate.

Table 6-1

Pollutants Which May be Present in Pharmaceutical Industry Wastewater

Conventional Pollutants		Nonconventional Pollutants
BOD_5	Oil & Grease	Acetaldehyde
pH	Fecal Coliform	Acetic acid
TSS		Acetone
		Acetonitrile
Priority Pollutants		Acetophenone
		Allyl chloride
Acrolein		4-Aminobiphenyl
Acrylonitrile		Ammonia
Benzene		n-Amyl acetate
Benzidine		Amyl alcohol
Bromoform		Aniline
Bromomethane		Benzaldehyde
Chlorobenzene		Benzotrichloride
Chloroethane		Benzyl alcohol
Chloroform		Benzyl chloride
Chloromethane		Benzyl bromide
Cyanide		Biphenyl
1,1-Dichloroethane		Bis(chloromethyl)ether
1,2-Dichloroethane		2-Bromo-Propanoylbromide
1,1-Dichloroethene		2-Butanone (MEK)
1,2-Dichloropropane		n-Butyl acetate
Ethylbenzene		n-Butyl alcohol
Hexachlorocyclopentadiene		tert-Butyl alcohol
Hexachloroethane		sec-Butyl alcohol
Methylene chloride		n-Butylamine
Nitrobenzene		Carbon disulfide
2-Nitrophenol		Catechol
4-Nitrophenol		Chloroacetic acid
o-Dichlorobenzene		2-Chloroacetophenone
p-Dichlorobenzene		3-Chloro-4-Fluoroaniline
Phenol		Chloromethyl methyl ether
1,1,2,2-Tetrachloroethane		COD (Chemical Oxygen Demand)
Tetrachloromethane		
Toluene		Cresol (Mixed)
1,1,1-Trichloroethane		Cumene
Trichloroethylene		Cyclohexane
1,1,2-Trichloroethane		Cyclohexanone
Vinyl chloride		Cyclopentanone

Table 6-1

(Continued)

Nonconventional Pollutants (Continued)	
Cyclohexylamine	Iodomethane
1,2-Dibromoethane	Isobutyraldehyde
1,2-trans-Dichloroethene	Isopropyl ether
Diethylaniline	Isopropanol
Diethyl ether	Isopropyl acetate
Diethylamine	Isobutyl alcohol
Diethyl carbonate	Methanol
Diethyl-ortho formate	Methyl cellosolve
Dimethylamine	Methyl amine
1,1-Dimethylhydrazine	Methyl formate
N,N-Dimethylacetamide	2-Methyl pyridine
N,N-Dimethylformamide	2-Methoxyaniline
N,N-Dimethylaniline	Methyl methacrylate
Dimethylcarbamyl chloride	Methyl-t-butyl-ether
Dimethyl sulfoxide	Methylal
1,4-Dioxane	Methyl isobutyl ketone (MIBK)
N-Dipropylamine	N-Nitrosomorpholine
Epichlorohydrin	n-Octane
Ethanol	n-Pentane
Ethylene oxide	Petroleum naphtha
Ethylamine	Polethylene glycol 600
Ethyl bromide	1,3-Propane sulfone
Ethyl cellosolve	n-Propanol
Ethyl acetate	B-Propiolactone
Ethylene glycol	Propionaldehyde
Ethyl cyanide	1,2-Propyleneimine
Formaldehyde	Propylene oxide
Formamide	Pyridine
Formic acid	Styrene
Furfural	Tetrachloroethene
Glycol ethers	Tetrahydrofuran
n-Heptane	Trichlorofluoromethane
2-Hexanone	2,4,5-Trichlorophenol
n-Hexane	Triethylamine
Hydrazine	Vinyl acetate
Iodoethane	Xylenes

Table 6-2

Pollutant Selection Evaluation Criteria for Pollutants Discharged by the Pharmaceutical Manufacturing Industry

Constituent Code	Constituent Name	Constituent Type (a)	Quantity Discharged (lbs/yr) (b)	Percent of Total Loading	# of Facilities Reporting Constituents	Hazard Score	Method Type (c)
97	Methanol (Methyl Alcohol)	N	15,388,273	28	82	2	GC
70	Ethanol	N	6,802,384	12	97	0	GC
118	Acetone	N	4,573,766	8.4	55	0	GCMS
94	Isopropanol	N	4,565,370	8.4	85	2	GC
2	Acetic acid	N	4,328,691	7.9	44	2	GC
102	Methylene chloride	P	3,590,640	6.6	47	5	GCMS
81	Formic acid	N	2,136,059	3.9	9	0	HPLC
9	Ammonium hydroxide	N	1,365,741	2.5	32	2	DIST
60	N,N-Dimethylacetamide	N	1,046,333	1.9	7	5	GCMS
130	Toluene	P	783,364	1.4	43	-5	GCMS
101	Methyl cellosolve	N	758,637	1.4	4	8	GC
66	Dimethyl sulfoxide	N	753,157	1.4	14	5	GCMS
27	N-Butyl alcohol	N	675,189	1.2	18	2	GC
61	Dimethylamine	N	661,605	1.2	3	2	HPLC
105	Methyl isobutyl ketone (MIBK)	N	635,677	1.2	9	0	GCMS
136	Triethylamine	N	633,225	1.2	15	2	HPLC
26	N-Butyl acetate	N	512,926	0.94	3	0	GCMS
64	N,N-Dimethylformamide	N	494,837	0.91	22	5	GCMS

Table 6-2

(Continued)

Constituent Code	Constituent Name	Constituent Type (a)	Quantity Discharged (lbs/yr) (b)	Percent of Total Loading	# of Facilities Reporting Constituents	Hazard Score	Method Type (c)
129	Tetrahydrofuran	N	478,669	0.88	17	3	GCMS
3	Acetonitrile	N	433,041	0.79	16	3	GCMS
37	Chloroform	P	409,317	0.75	17	10	GCMS
71	Ethyl acetate	N	390,584	0.72	27	0	GC
79	Formaldehyde	N	334,527	0.61	27	10	HPLC
10	n-Amyl acetate	N	293,408	0.54	5	0	GCMS
113	Petroleum naphtha	N	261,137	0.48	3	3	GC
77	Ethylene glycol	N	225,188	0.41	10	5	GC
55	Diethylamine	N	219,374	0.40	7	2	HPLC
124	Pyridine	N	212,581	0.39	10	7	GCMS
11	Amyl alcohol	N	197,635	0.36	6	2	GC
95	Isopropyl acetate	N	184,550	0.34	9	0	GCMS
103	Methyl formate	N	157,727	0.29	3	0	GC
39	Chloromethane	P	141,416	0.26	3	5	GCMS
29	Tert-Butyl alcohol	N	121,408	0.22	5	0	GC
15	Benzene	P	121,400	0.22	1	5	GCMS
139	Xylenes	N	53,724	0.098	14	0	GCMS
106	2-Methylpyridine	N	48,800	0.089	1	0	GCMS
43	Cyclohexane	N	44,183	0.081	6	-3	GC

Table 6-2

(Continued)

Constituent Code	Constituent Name	Constituent Type (a)	Quantity Discharged (lbs/yr) (b)	Percent of Total Loading	# of Facilities Reporting Constituents	Hazard Score	Method Type (c)
93	Isobutyraldehyde	N	35,659	0.065	2	0	HPLC
115	Polyethylene glycol 600	N	31,219	0.057	8	0	HPLC
84	N-Heptane	N	28,044	0.051	12	1	GCMS
51	1,2-Dichloroethane	P	27,559	0.051	6	14	GCMS
67	1,4-Dioxane	N	24,927	0.046	6	12	GCMS
99	Methylamine	N	23,717	0.043	4	0	HPLC
48	o-Dichlorobenzene	P	21,499	0.039	2	-3	GCMS
62	N,N-Dimethylaniline	N	19,155	0.035	2	5	GCMS
25	2-Butanone (MEK)	N	17,426	0.032	4	0	GCMS
82	Furfural	N	15,406	0.028	2	7	HPLC
58	Diethyl ether	N	14,810	0.027	9	0	GCMS
83	Glycol ethers	N	14,483	0.027	6	5	NA
96	Isopropyl ether	N	12,387	0.023	5	-5	GCMS
117	N-Propanol	N	12,238	0.022	5	2	GC
87	N-Hexane	N	11,265	0.021	9	2	GCMS
22	Bis(Chloromethyl)ether	N	11,221	0.021	1	14	GCMS
114	Phenol	P	10,974	0.020	12	7	GCMS
80	Formamide	N	7,544	0.014	4	0	HPLC
134	Trichlorofluoromethane	N	5,771	0.011	2	-5	GCMS

Table 6-2

(Continued)

Constituent Code	Constituent Name	Constituent Type (a)	Quantity Discharged (lbs/yr) (b)	Percent of Total Loading	# of Facilities Reporting Constituents	Hazard Score	Method Type (c)
35	Chlorobenzene	P	5,616	0.010	4	-2	GCMS
12	Aniline	N	4,603	0.0084	4	19	GCMS
63	Dimethylcarbamyl chloride	N	3,973	0.0073	1	5	GCMS
132	1,1,2-Trichloroethane	P	2,954	0.0054	2	14	GCMS
111	n-Octane	N	2,200	0.0040	1	6	GCMS
56	Diethylaniline	N	1,703	0.0031	1	2	GCMS
45	Cyclohexylamine	N	1,250	0.0023	1	2	GCMS
31	Carbon disulfide	N	1,100	0.0020	1	-5	GCMS
123	Propylene oxide	N	1,068	0.0019	1	14	GCMS
78	Ethylene oxide	N	1,015	0.0019	3	14	GCMS
91	Iodomethane	N	996	0.0018	2	-5	GCMS
14	Benzaldehyde	N	896	0.0016	3	5	NA
33	Chloroacetic acid	N	870	0.0016	2	10	GCMS
30	N-Butylamine	N	804	0.0015	2	2	HPLC
44	Cyclohexanone	N	738	0.0013	1	2	GCMS
46	Cyclopentanone	N	678	0.0012	1	2	GCMS
100	Methyl-t-butyl-ether	N	590	0.0011	2	0	GCMS
98	Methylal	N	541	0.00099	1	0	HPLC
72	Ethylamine	N	466	0.00086	1	2	HPLC

Table 6-2

(Continued)

Constituent Code	Constituent Name	Constituent Type (a)	Quantity Discharged (lbs/yr) (b)	Percent of Total Loading	# of Facilities Reporting Constituents	Hazard Score	Method Type (c)
18	Benzyl alcohol	N	446	0.00082	16	2	GCMS
126	1,1,2,2-Tetrachloroethane	P	121	0.00022	1	12	GCMS
131	1,1,1-Trichloroethane	P	98	0.00018	4	-5	GCMS
73	Ethylbenzene	P	90	0.00016	1	-5	GCMS
74	Ethyl bromide	N	65	0.00012	2	-5	GC
75	Ethyl cellosolve	N	60	0.00011	1	NA	GCMS
20	Benzyl chloride	N	50	9.2E-05	2	12	GC
92	Isobutyl alcohol	N	46	8.4E-05	1	0	GCMS
89	Hydrazine	N	37	6.8E-05	2	22	HPLC
1	Acetaldehyde	N	33	6.1E-05	1	10	HPLC
7	Allyl chloride	N	5	<0.00001	1	-3	GCMS
6	Acrylonitrile	P	1	<0.00001	1	17	GCMS
128	Tetrachloromethane	P	1	<0.00001	1	7	GCMS

(a) N - Nonconventional Pollutant
P - Priority Pollutant

(b) Quantity discharged is equal to the sum of air emissions from wastewater prior to discharge (lbs) and discharge to surface water and/or sewer (lbs) from Table 3-2 of the Detailed Questionnaire.

(c) GC - Gas Chromatography
GCMS - Gas Chromatography Mass Spectrometry
HPLC - High Performance Liquid Chromatography
DIST - Distillation
NA - No Methods Available

Table 6-3

Priority Pollutants Not Selected for Regulation in the Pharmaceutical Manufacturing Industry

Pollutant	Reason for Exclusion
Acrylonitrile	Discharged in trace amounts from one facility (1 lb/yr)
Tetrachloromethane	Discharged in trace amounts from one facility (1 lb/yr)
Ethylbenzene	Discharged in trace amounts from one facility (90 lbs/yr), low toxicity
1,1,1-Trichloroethane	Discharged in trace amounts (98 lbs/yr), low toxicity
1,1,2,2-Tetrachloroethane	Discharged in low amounts from one facility (121 lbs/yr)
1,1,2-Trichloroethane	Discharged in low amounts from two facilities (2,954 lbs/yr)

Table 6-4

Nonconventional Pollutants Not Selected for Regulation in the Pharmaceutical Manufacturing Industry

Pollutant	Reason for Exclusion
Allyl chloride	Discharged in trace amounts from one facility (5 lbs/yr), low toxicity
n-Octane	Discharged in low amounts from one facility (2,200 lbs/yr), low toxicity
Diethylaniline	Discharged in low amounts from one facility (1,703 lbs/yr), low toxicity
Cyclohexylamine	Discharged in low amounts from one facility (1,250 lbs/yr), low toxicity
Carbon disulfide	Discharged in low amounts from one facility (1,100 lbs/yr), low toxicity
Propylene oxide	Discharged in low amounts from one facility (1,068 lbs/yr)
Iodomethane	Discharged in low amounts from two facilities (996 lbs/yr), low toxicity
Chloroacetic acid	Discharged in low amounts from two facilities (870 lbs/yr), low toxicity
n-Butylamine	Discharged in low amounts from two facilities (804 lbs/yr), low toxicity
Cyclohexanone	Discharged in low amounts from one facility (738 lbs/yr), low toxicity
Cyclopentanone	Discharged in low amounts from one facility (678 lbs/yr), low toxicity
Methyl-t-butyl-ether	Discharged in low amounts from two facilities (590 lbs/yr), low toxicity
Methylal	Discharged in low amounts from one facility (541 lbs/yr), low toxicity
Ethylamine	Discharged in low amounts from one facility (466 lbs/yr), low toxicity
Ethyl bromide	Discharged in trace amounts from two facilities (65 lbs/yr), low toxicity
Ethyl cellosolve	Discharged in trace amounts from one facility (60 lbs/yr)
Benzyl chloride	Discharged in trace amounts from two facilities (50 lbs/yr)
Isobutyl alcohol	Discharged in trace amounts from one facility (46 lbs/yr), low toxicity
Hydrazine	Discharged in trace amounts from two facilities (37 lbs/yr)
Acetaldehyde	Discharged in trace amounts from one facility (33 lbs/yr)
Acetic acid	Addressed by pH control under BPT
Formic acid	Addressed by pH control under BPT
Benzaldehyde	Discharged in low amounts (896 lbs/yr), low toxicity
Benzyl alcohol	Discharged in low amounts (446 lbs/yr), low toxicity
Ethylene oxide	Discharged in low amounts (1,015 lbs/yr)
Glycol ethers	No analytical method available
Dimethyl carbamyl chloride	Hydrolysis/does not persist in water
Bis(chloromethyl)ether	Hydrolysis/does not persist in water

REFERENCES

1. Natural Resources Defense Council, Inc, et al., v. Russel E. Train, 8 ERC 2120 (D.D.C. 1976) modified and Natural Resources Defense Council, Inc., et al., v. Douglas M. Costle, 12 ERC 1833 (D.D.C. 1979).

2. U.S. EPA, Office of Water Regulations and Standards. Preliminary Data Summary for the Pharmaceutical Manufacturing Point Source Category, EPA 440/1-89/084, U.S. Environmental Protection Agency, Washington, D.C. September 1989.

3. Radian Corporation Memorandum Basis of Water-Related Hazard Rankings, February 4, 1994.

SECTION 7

REGULATORY OPTIONS

7.1 Introduction

This section presents the regulatory options considered by the Agency for proposal of BPT, BCT, BAT, NSPS, PSES and PSNS effluent limitations guidelines and standards for the pharmaceutical manufacturing industry. The following information is presented in this section:

- Section 7.2 discusses the pollution prevention measures and major wastewater treatment technologies used by the industry; and
- Section 7.3 discusses the development of control and treatment options.

7.2 Pollution Prevention Measures and Wastewater Treatment Technologies in the Pharmaceutical Manufacturing Industry

This section describes pollution prevention practices and major wastewater treatment technologies used in the pharmaceutical manufacturing industry according to responses to the Detailed Questionnaire. Section 7.2.1 defines pollution prevention and describes how pollution prevention techniques are implemented in the industry. Sections 7.2.2 through 7.2.8 describe the major wastewater treatment technologies used in the industry based on responses to the Detailed Questionnaire. These treatment technologies include:

- Advanced biological treatment (Section 7.2.2):
- Multimedia filtration (Section 7.2.3);
- Polishing pond treatment (Section 7.2.4);
- Cyanide destruction (Section 7.2.5);

- Steam Stripping and Distillation (Section 7.2.6);
- Granular activated carbon adsorption (Section 7.2.7);
- pH adjustment/neutralization (Section 7.2.8);
- Equalization (Section 7.2.9);
- Air stripping (Section 7.2.10); and
- Incineration (Section 7.2.11).

Each technology section includes a general description of how the technology works, what types of pollutants the technology treats, and how the pharmaceutical manufacturing industry currently uses the technology.

Table 7-1 presents the total number of facilities (out of the 244 facilities responding to the Detailed Questionnaire) that reported using each of these major technologies.

7.2.1 Pollution Prevention

The Agency examined pollution prevention practices in an effort to incorporate pollution prevention into the regulatory options developed. Although shown to be effective at reducing pollutant loadings and volumes of wastes generated at pharmaceutical manufacturing facilities, pollution prevention measures were not incorporated into the various technology options considered as bases for the proposed limitations and standards because of obstacles specific to the pharmaceutical manufacturing industry. However, the Agency believes that numerous facilities will choose to integrate pollution prevention practices into a cost-effective strategy to comply with the proposed effluent limitations guidelines and standards, where site-specific circumstances allow them to do so. This section provides a general description of pollution prevention as it applies to the pharmaceutical manufacturing industry, and discusses the Agency's efforts to incorporate pollution prevention into the regulatory development process.

7.2.1.1 General Description

Pollution prevention is defined as the use of materials, processes, or practices that reduce or eliminate the creation of pollutants or wastes at the source. Also known as source reduction, pollution prevention includes practices that reduce the use of hazardous and nonhazardous materials, energy, water, or other natural resources. With the Pollution Prevention Act of 1990, Congress established pollution prevention as a national policy, declaring that the creation of pollutants should be prevented or reduced during the production cycle whenever feasible. (1)

Pollution prevention in the manufacturing community can be achieved by changing production processes to reduce or eliminate the generation of waste at the source. Pollution control and waste handling measures (including waste treatment, off-site recycling, volume reduction, dilution, and transfer of constituents to another environmental medium) are not considered pollution prevention because such measures are applied only after wastes are generated.(1)

The Pollution Prevention Act of 1990 and EPA's 1991 Pollution Prevention Strategy establish an environmental management hierarchy that includes (in order of highest priority): source reduction, recycling, treatment, and disposal or release.(1) Essentially, the environmental hierarchy establishes a set of preferences, rather than an absolute judgment, that source reduction is always the most desirable option. Adoption of the source reduction option, for example, depends on applicable regulatory requirements, achievable levels of risk reduction, and cost effectiveness. As it applies to industry, the environmental management hierarchy stipulates that:

- Pollution should be reduced at the source whenever feasible;
- Pollution that cannot be reduced should be recycled in an environmentally safe manner whenever feasible;

- Pollution that cannot be reduced or recycled should be treated in an environmentally safe manner whenever feasible; and
- Disposal or other release into the environment should be used only as a last resort and should be conducted in an environmentally safe manner.

Figure 7-1 outlines the environmental management hierarchy, as applied to industry.

Examples of current pollution prevention initiatives in the pharmaceutical manufacturing industry are documented in the U.S. EPA Pollution Prevention Information Clearinghouse (PPIC). Source reduction was achieved at one plant by substituting a water-based material for an organic solvent-based material used to coat medicine tablets. This process change reduced organic air emissions by 24 tons/year, eliminated potential risks associated with solvent inhalation by workers, saved organic solvent purchase costs, avoided potential costs for complying with emission standards, and resulted in a payback period of less than one year.

Another plant used conventional separation processes to recover and reuse 70% of the acetone contained in the plant wastewater. Prior to recycling, the plant discharged wastewater containing approximately 200,000 lb/yr of acetone to a POTW. By recycling the acetone, the facility saves approximately $70,000 in annual treatment costs, reduces the amount of acetone purchased, and reduces liabilities by generating less waste.

7.2.1.2 Efforts to Incorporate Pollution Prevention during the Regulatory Development Process

As demonstrated in the previous examples, pollution prevention initiatives can reduce the toxicity and volume of a pharmaceutical manufacturing facility's waste while lowering liability risk and operating costs. With such benefits in mind, EPA's Office of Water has been working with the Food and Drug Administration (FDA) and EPA's Office of

I. Source Reduction

A. Product Changes
- Design for Less Environmental Impact
- Increase Product Life

B. Process Changes

1. Input Material Changes
   - Material Purification
   - Substitution of Less Toxic Materials

2. Technology Changes
   - Layout Changes
   - Increased Automation
   - Improved Operating Conditions
   - Improved Equipment
   - New Technology

3. Improved Operating Practices
   - Operating and Maintenance Procedures
   - Management Practices
   - Stream Segregation
   - Material Handling Improvements
   - Production Scheduling
   - Inventory Control
   - Training
   - Waste Segregation

II. Recycling

A. Reuse

B. Reclamation

III. Treatment

IV. Disposal

Reference: United States EPA, Office of Research and Development. Facility Pollution Prevention Guide, EPA/600/R-92/088, May 1992.

Figure 7-1. Environmental Management Options Hierarchy

Pollution Prevention and Toxics (OPPT) to incorporate pollution prevention into the proposed pharmaceutical manufacturing industry effluent limitations guidelines and standards.

Prior to the implementation of a new drug manufacturing process, the manufacturer must submit a new drug application to the FDA. During its review of a new drug application, the FDA assesses the safety, efficacy, and quality of the drug. The FDA also examines the safety to the human environment from the manufacture and use of the drug. This examination includes an environmental assessment, review of clinical trials and animal trials of the drug. The FDA will also assess other factors such as the stability of the drug (shelf life) and the extent of drug absorption into the bloodstream.

Prior to the implementation of a change in a drug manufacturing process, that has already been approved by the FDA, a manufacturer must submit a supplement application to the FDA. During its review of a supplement application, the FDA assesses whether the proposed process change will produce a drug that equals or surpasses the efficacy and quality of the drug which was produced using the initial (unaltered) manufacturing process.

Currently, EPA's Office of Water is working with the FDA to explore the potential for pharmaceutical manufacturers to reduce the use of solvents in manufacturing operations and thereby minimize solvent loadings in manufacturing wastewaters. In the past, the length of time required by FDA to review and approve supplement applications (i.e., applications that propose changes to existing pharmaceutical manufacturing processes) has deterred the implementation of pollution prevention measures. However, since the enactment of the "Prescription Drug User Fee Act of 1992," 21 U.S.C. 379 et seq., Pub. L. 102-571, October 29, 1992, the FDA has committed to using the revenues generated under that Act to expedite the prescription drug review and approval process, including expediting decisions on supplements relating to pollution prevention-oriented process changes. FDA expects to eliminate its backlog of applications, amendments and

supplements by 1994 and to achieve, by Fiscal Year 1997, its goal of reviewing and acting upon every complete application, amendment and supplement within six months of submission. EPA believes that such expeditious processing of supplements will eliminate impediments that presently discourage pharmaceutical plants from making process changes necessary to achieve source reductions. Additionally, EPA has transferred information collected from the pharmaceutical manufacturing industry via the Detailed Questionnaire to FDA, as stated in the August 23, 1993 Federal Register Notice (58 FR 44519). This information will enable FDA to develop a list of processes that could be the subject of supplement applications.

The Office of Water also worked with OPPT to develop Section 3b of the Detailed Questionnaire. This section contains questions pertaining to waste minimization/ pollution prevention efforts implemented at each facility in 1990. Two hundred and eighty Detailed Questionnaires were sent to pharmaceutical manufacturing facilities in 1991, and responses were received from 244 facilities. Three of the 244 facilities that responded to the questionnaire gave no response to Section 3b. Eighty-nine of the 244 facilities indicated that they had no pollution prevention programs in place. One hundred and fifty-two of the 244 facilities claimed to have a pollution prevention program in place on site. Ninety of the 152 facilities with pollution prevention programs in place reported that their program did not include their pharmaceutical manufacturing processes. Sixty-two of the 152 facilities reported that the pollution prevention program implemented on site included their pharmaceutical manufacturing processes.

The 62 facilities that identified pollution prevention programs relevant to their pharmaceutical manufacturing processes reported 89 specific waste minimization/ pollution prevention activities implemented at their facilities in 1990, and described these

activities in the Detailed Questionnaire. The types of activities undertaken are summarized below.

Source Reduction				Number of Recycling Activities Reuse/Reclamation	Total Activities
	Number of Process Changes				
Number of Product Changes	Input Material Changes	Technology Changes	Improved Operating Practices		
3	22	16	16	32	89

Examples of pollution prevention activities reported by pharmaceutical manufacturing facilities include the following:

- **Product Changes** - Eliminate product packaging, and reformulate vitamin product filmcoats to remove volatile organic pollutants.
- **Input Material Process Changes** - Eliminate and/or reduce acetic acid, acetone, aerosols, chloroform, methanol, methylene chloride, toluene, and 1,1,1-trichloroethane from various production processes.
- **Technology Process Changes** - Install solvent recovery units; implement automated cleaning system for wastewater reduction; design closed-loop solvent recovery units for all new processes; and replace solvent-based cleaning units with water-based cleaning units.
- **Improved Operating Practices** - Separate nonquality products from batches earlier in production process; improve reclamation systems and distillation capabilities; combine solvent waste streams to avoid need for multiple recovery systems; and reduce overall waste solvent generation.
- **Recycling/Reuse Activities** - Recycle/reuse alcohol, aqueous ammonia, dicyclohexylamine, dimethylaniline, freon, packaging materials, plastics, solvents, spent nickel catalyst wastes, steel drums, treated wastewater, 1,1,2-trichloroethane, triethylamine, and wooden pallets.

In addition to reporting pollution prevention activities, pharmaceutical manufacturing facilities reported quantities of chemicals that were recycled/reused. Table 7-2 summarizes the quantity of chemicals recycled/reused by pharmaceutical manufacturing facilities during 1990, as reported in the Detailed Questionnaire responses. As shown in the table, a total of approximately 335,000,000 pounds of 15 different chemicals were recycled/reused at the facilities during 1990.

The diversity of reported pollution prevention activities and recycled/reused chemicals demonstrate the facility-specific and/or process-specific nature of pollution prevention initiatives. Many of the examples listed are applicable to specific manufacturing processes and are not transferable to other operations. As reported in Section 3b of the Detailed Questionnaire, pollution prevention opportunities are generally site- and process-specific in the pharmaceutical manufacturing industry.

Pollution prevention has been shown to be an effective means of reducing pollutant loadings and volumes of wastes generated during manufacturing processes. Pollution prevention initiatives, however, are not part of the technology basis of the proposed regulatory options for the pharmaceutical manufacturing industry because of several important constraints. First, FDA review and approval is required before any modifications in manufactured pharmaceutical products or pharmaceutical manufacturing processes are permitted. EPA determined that it was not appropriate to include process modifications as part of the basis for regulatory options, when such modifications would need to be reviewed and approved by FDA on a case-by-case basis. Second, the pharmaceutical manufacturing industry is complex and varied, and, therefore, EPA determined that the pollution prevention opportunities that exist are facility-, process-, and product-specific. EPA did not identify any specific pollution prevention techniques that could be incorporated into regulatory options and applied on a category- or subcategory-wide basis.

However, in addition to evaluating opportunities for source reduction, EPA also examined potential treatment technologies to determine whether any might promote recovery, recycling, and reuse of process wastewater generated by pharmaceutical manufacturing operations, such as solvents. After evaluating the various technologies available to treat volatile-laden wastewaters, EPA concluded that in-plant technologies such as steam stripping/distillation offered the best opportunity for recovery of solvents from wastewater. Steam stripping/distillation in plant not only avoids the dilution effects of commingling process wastewater streams and the transfer of volatile pollutants to air associated with other technologies, but it also allows the pharmaceutical manufacturing operation to recover the stripped solvents from the treatment process in an efficient and cost-effective manner from concentrated streams. These recovered solvents can then be recycled back into the process from which they were removed, reused in other manufacturing operations (e.g., in this industry or in other industries), or reused as "clean fuel" for boilers or other combustion devices. For a discussion of "clean fuels," see Section 12.4.3.

Thus, the Agency believes that the proposed regulation will foster the implementation of pollution prevention and recycle/reuse initiatives even though pollution prevention measures are not specifically part of the technologies upon which the proposed limitations and standards are based. Numerous facilities would use pollution prevention measures that reduce pollutant loadings and volumes of waste generated as part of a cost-effective strategy to comply with the proposed effluent limitations guidelines and standards. In addition, while not currently proposing specific best management practices (BMPs), EPA is evaluating the use of BMPs for the pharmaceutical industry as described in Appendix B and these activities could include pollution prevention types of activities.

7.2.2 Advanced Biological Treatment

7.2.2.1 General Description

Advanced biological treatment is used in the pharmaceutical manufacturing industry to treat BOD_5, COD, TSS, and to degrade various organic constituents. The term "advanced" is used to refer to treatment systems that consistently surpass, on a long-term basis, 90% BOD_5 reduction and 74% COD reduction in pharmaceutical manufacturing wastewater, as required by the existing BPT effluent limitations guidelines (40 CFR Part 439). To be considered advanced, treatment systems must also provide reduction of ammonia in the wastewater through nitrification, where necessary.

Biological systems can be divided into two basic types: aerobic (treatment takes place in the presence of oxygen) and anaerobic (treatment takes place in the absence of oxygen). According to responses to the Detailed Questionnaire, only two pharmaceutical manufacturing facilities reported using anaerobic biological treatment systems. The four most common aerobic treatment technologies in the industry are activated sludge, aerated lagoon, trickling filter, and rotating biological contactor (RBC).

In aerobic biological treatment processes, oxygen-requiring microorganisms decompose organic and nonmetallic inorganic constituents into carbon dioxide, water, nitrates, sulfates, organic byproducts, and cellular biomass. The microorganisms are maintained by adding oxygen and nutrients (usually nitrogen and phosphorous) to the system. Activated sludge and aerated lagoon processes are suspended-growth processes in which the microorganisms are maintained in suspension within the liquid being treated. The trickling filter and RBC processes are attached-growth processes in which microorganisms grow on an inert medium (e.g., rock, wood, plastic). Three types of activated sludge processes were listed as choices in the Detailed Questionnaire: single, two-stage, and oxygen-activated sludge. Table 7-1 lists these processes under the heading

"Biological Treatment." As can be seen in the table, the majority of biological treatment systems used in the industry are activated sludge systems.

An activated sludge treatment system normally consists of an equalization basin, a settling tank (primary clarifier), an aeration basin, a secondary clarifier, and a sludge recycle line. Equalization of flow, pH, temperature, and pollutant loads is necessary to perform consistent, adequate treatment. The settling tank is used to remove settleable solids prior to aeration. The aerobic bacterial population is maintained in the aeration basin, in which oxygen, recycled sludge, and nutrients are added to the system. Oxygen is normally supplied by aerators that also provide mixing to help keep microorganisms in suspension. Recycled sludge is added to keep an optimal concentration of acclimated microorganisms in the aeration basin. The secondary clarifier controls the amount of suspended solids discharged, as well as provides sludge for recycle to the aeration basin (2). Sludge produced by these systems generally consists of biological waste products and expired microorganisms. This sludge may accumulate under certain operating conditions and may therefore require periodic removal from the aeration basin.

Generated sludge will require some type of storage, handling, and disposal. Biological sludges are normally treated in a two-step process prior to disposal: thickening followed by dewatering. Other sludge treatment may also be performed, but these processes are the most common. The goal for each of these operations is to decrease the overall volume of sludge. Thickening of waste-activated sludge is normally performed in one of three ways: gravity separation, dissolved-air flotation, or centrifuging. Generally, thickeners will increase the solids content of sludge from 1% (typical from biological treatment) to 4 or 5%. Sludge dewatering is normally performed using some type of filter, including filter presses, vacuum filters, and belt filters. These units normally can increase the solids content in sludge from 5% up to 15 to 30%, which greatly reduces the shipping, handling and disposal costs associated with sludge generation from a biological treatment unit. (3)

Ammonia treatment by nitrification is achieved in biological treatment units by incorporating two additional sets of autotrophic microorganisms. The first set of microorganisms converts ammonia to nitrites and the second set converts nitrites to nitrates. These microorganisms are maintained in the treatment tank in a similar fashion as the microorganisms described above (addition of oxygen, nutrients, etc).

Some key design parameters for activated sludge systems include nutrient-to-microorganism ratio, mixed liquor suspended solids (MLSS), sludge retention time, oxygen requirements, nutrient requirements, sludge production, substrate removal rate constant (K), and percent BOD_5 of effluent TSS. Pharmaceutical manufacturing industry averages for some of these parameters are presented in the following table.

Parameter	Subcategory A and C Average	Subcategory B and D Average
Food to Microorganism Ratio (lb/lb/day)	0.561	0.054
MLSS (mg/L)	5,521	3,443
Sludge Retention Time (hours)	33.0	22.9
K	11.14	2.06
%BOD_5 of TSS	23	24

7.2.2.2 Industry Application

Based on responses to the Detailed Questionnaire, 58 of 244 responding facilities in the pharmaceutical manufacturing industry use some form of activated sludge treatment process, 12 use aerated lagoons, 5 use trickling filters, and 3 use RBC treatment. Most of these facilities are operated at or near the facility off-site wastewater discharge point (end-of-pipe). There are no specific data regarding whether the treatment units are used primarily to reduce concentrations of conventional pollutants or organic constituents in the wastewater. However, it is likely that these systems were initially designed to treat BOD_5 and COD.

7.2.3 Multimedia Filtration

7.2.3.1 General Description

Multimedia filtration is used in the pharmaceutical manufacturing industry to reduce TSS in wastewater. This technology may also serve to treat BOD_5 in wastewater by removing BOD_5 associated with particulate matter. Multimedia filtration is performed by introducing a wastewater to a fixed bed of inert granular media. Suspended solids are removed from the wastewater by one or more of the following processes: straining, interception, impaction, sedimentation, and adsorption. This operation is continued until there is either solids "breakthrough" (solids concentration increases to an unacceptable level in the discharge from the bed), or the head loss across the bed becomes too great (due to trapped solids) to operate the bed efficiently.

If either of these conditions occurs, the bed must be cleaned by backwashing before it can be operated effectively again. Backwashing usually is accomplished by reversing the flow to the bed and introducing a "clean" stream of wash water. Wash water is introduced until the bed becomes fluidized (expanded). At this point, the solids are washed from the bed and carried away from the unit. It is common to return the backwashed solids stream to the biological treatment system (if applicable).

In multimedia filtration, a series of layers, each with a progressively smaller grain size medium (travelling from inflow to outflow of the bed) are used in the filtration bed. This design allows solids to penetrate deeper into the bed before becoming fixed, thus increasing the capacity of the bed and decreasing the buildup of head loss in the unit. Typical filtration media include garnet, crushed anthracite coal, resin beads, and sand. Though downflow (gravity flow) systems are the most common, upflow and biflow (influent is introduced above and below the filter medium, and the effluent discharges from the center of the filter medium) filtration units can also be used. Figure 7-2 shows a cross-section of a typical downflow, multimedia filtration bed. (3)

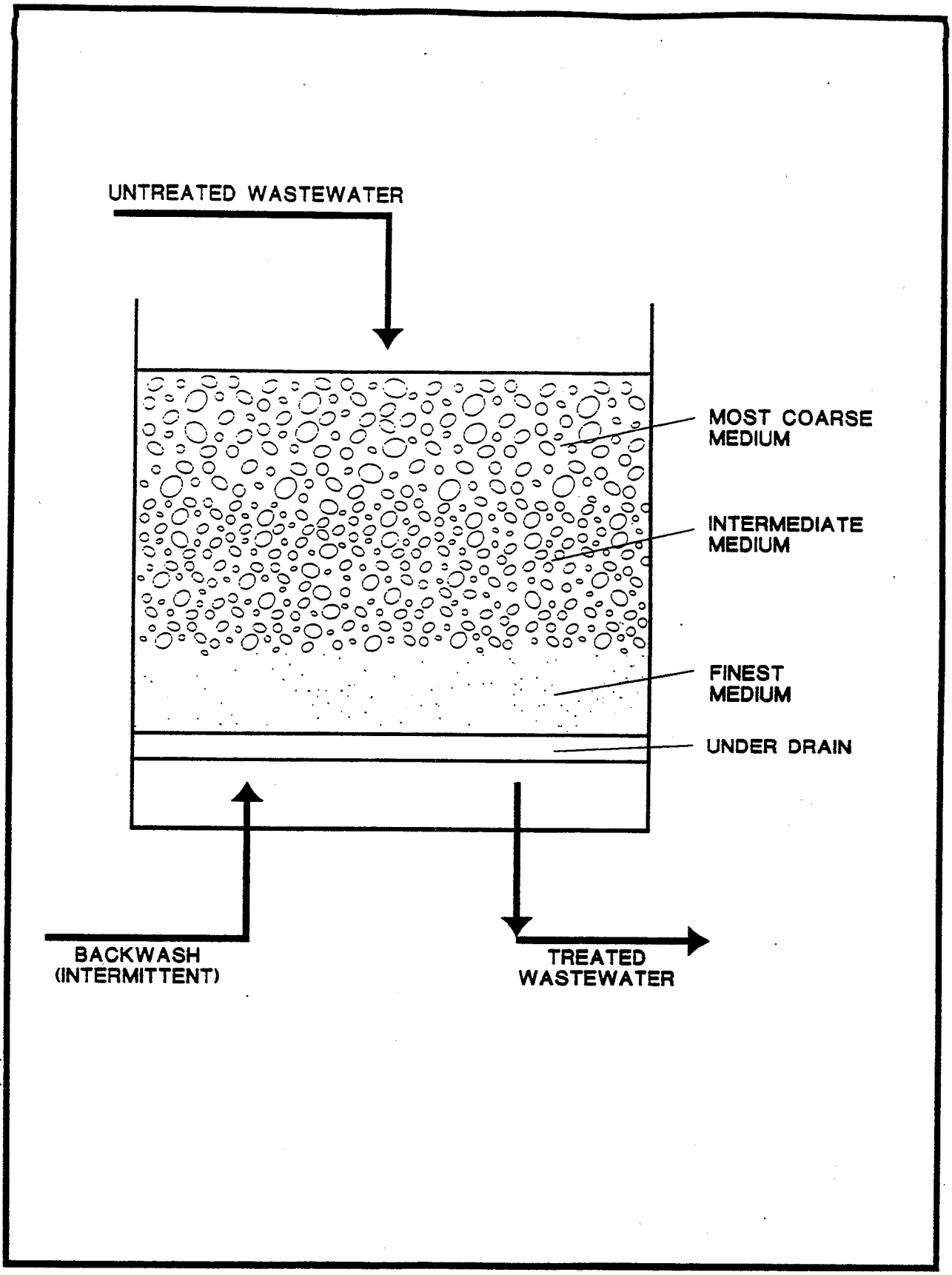

Figure 7-2. Typical Downflow Multimedia Filter Bed

Some key design parameters associated with multimedia filtration units include wastewater flow rate, hydraulic loading rate, and filter medium depth. The following table shows ranges of values for each of these parameters for treatment units currently operated in the pharmaceutical manufacturing industry.

Parameter	Range	Units
Flow Rate	0.03 - 2.18	MGD
Hydraulic Loading Rate	2.0 - 5.0	gpm/ft^2
Depth of Medium	6 - 72	inches

7.2.3.2 Industry Application

Based on responses to the Detailed Questionnaire, 6 of 244 responding pharmaceutical manufacturing facilities use multimedia filtration treatment. This treatment is generally performed after biological treatment (if applicable) for additional TSS removal prior to wastewater discharge. Multimedia filtration can also provide limited treatment of BOD_5 by removing the BOD_5 load associated with suspended solids. The following is the breakdown of specific applications of multimedia filtration treatment in the industry: four facilities use multimedia filtration as a tertiary wastewater treatment, one facility uses it to treat noncontact cooling water prior to recycle, and one facility uses it as a treatment prior to granular activated carbon (GAC) treatment.

7.2.4 Polishing Pond

7.2.4.1 General Description

Polishing ponds are used in the pharmaceutical manufacturing industry to remove TSS from wastewater using gravity settling. Some BOD_5 removal associated with the settling of suspended solids may also occur.

The wastewater is introduced at one end of the pond and ultimately flows out the other end. The pond is designed such that the water retention time is high enough and the water is still enough to allow solids to fall out of suspension. If the flow is too fast, or other mixing is added to the system, solids may be maintained in suspension and discharged from the pond.

To avoid anaerobic conditions in the bottom portion of the pond, these units must be designed to be shallow, which may require a large land area if flow to the unit is high. Depths of polishing ponds currently used in the industry range from 2.5 to 14 feet. Retention times range from 0.2 to 14.6 days. In the past, polishing ponds have been designed with an earthen liner only; however, current regulations require installation of a minimum of two liners and a leak detection system (40 CFR 264.221) for most new applications to this industry. Polishing ponds will accumulate solids over time and will therefore require periodic cleanout.

7.2.4.2 Industry Application

Based on responses to the Detailed Questionnaire, 8 of 244 responding pharmaceutical manufacturing facilities use polishing ponds to treat wastewater. This treatment is not currently common in the industry, and because of increasing regulatory requirements governing the use of ponds (surface impoundments), facilities have limited plans for installation of more of these units. For the facilities that use polishing ponds, this technology is generally used to treat wastewater just prior to off-site discharge.

7.2.5 Cyanide Destruction

7.2.5.1 General Description

Several cyanide destruction treatment technologies are currently used in the pharmaceutical manufacturing industry, including alkaline chlorination, hydrogen

peroxide oxidation, and basic hydrolysis. The alkaline chlorination treatment process involves reacting free cyanide with hypochlorite (formed by reacting chlorine gas with an aqueous sodium hydroxide solution) to form nitrogen and carbon dioxide. The reaction is a two-step process and is normally performed separately in two reactor vessels. Because treatment is normally performed in batches, it is necessary to use an additional equalization tank to store accumulated wastewater during treatment. The reactors need to be equipped with agitators, and both reaction steps require close monitoring of pH and oxidation/reduction potential (ORP). These reactions are normally performed at ambient temperatures. (4)

Hydrogen peroxide treatment involves adding hydrogen peroxide to cyanide-bearing wastewater to convert free cyanide to ammonia and carbonate ions. This treatment is normally performed batch-wise in a reaction vessel or vessels. The treatment process consists of heating the wastewater to approximately 125°F and adjusting the pH in the reaction vessel to approximately 11. Hydrogen peroxide is added to the vessel and is allowed to react for approximately one hour. Required equipment for this process includes reaction vessel(s), storage vessels for hydrogen peroxide and a pH adjustment compound (typically sodium hydroxide), an equalization tank, and feed systems for hydrogen peroxide and sodium hydroxide.(4)

Hydrolysis treatment involves reacting free cyanide with water under basic conditions to produce formate and ammonia. This process requires approximately one hour to proceed and is typically performed at a temperature between 170 and 250°C, and at a pH of between 9 and 12. Hydrolysis is normally performed in a reactor vessel equipped with a heat exchanger and a system to store and deliver sodium hydroxide (or other basic compound).

7.2.5.2 Industry Application

Based on responses to the Detailed Questionnaire, 10 of 244 responding pharmaceutical manufacturing facilities use cyanide destruction treatment. Of these, six use alkaline chlorination, three use hydrogen peroxide oxidation, and one uses hydrolysis. Most of these facilities apply the cyanide destruction technologies in the process area that generates the cyanide-bearing wastewater, and most of the treatment units are operated in batch mode.

7.2.6 Steam Stripping and Distillation

Steam stripping and distillation are used both in industrial chemical production (for chemical recovery and/or recycle) and in industrial waste treatment to remove gases and/or organic chemicals from wastewater streams by providing steam to a tray or packed column. Under both technologies, differences in relative volatility between the organic chemicals and water are used to achieve a separation. The more volatile components of the feed mixture concentrate in the vapor, while the less volatile components concentrate in the liquid residue (bottoms). Steam stripping and distillation are effective treatment for a wide range of aqueous streams containing organics and ammonia. Appropriately designed and operated columns can treat a variety of waste streams ranging from wastewaters containing a single volatile constituent to complex organic/inorganic mixtures. Steam stripping and distillation can be used both as in-plant processes to recover concentrated organics from aqueous streams and as end-of-pipe treatment to remove organics from wastewaters prior to discharge or recycle. For most effective wastewater treatment, columns should be placed after the process generating the wastewater and before the wastewater is combined with other wastewater that does not contain the pollutants being treated. Wastewater with high concentration and low flow is easier and less expensive to treat than wastewater with high flow and/or low concentration. In addition, the amount of volatiles emitted to the air can be minimized if columns are placed prior to exposure of the wastewater stream to the atmosphere.

7.2.6.1 General Description

Steam stripping and distillation can be conducted as either a batch or continuous operation in a packed tower or fractionating column (sieve tray or bubble cap) with more than one stage of vapor-liquid contact. In a steam stripping column, the wastewater feed enters near the top of the column and then flows downward by gravity, countercurrent to the steam which is introduced at the bottom of the column. In a distillation column, the wastewater feed enters lower down the column to allow for a rectification section above the feed. In the rectification section, a portion of the condensed vapors are refluxed to the column to countercurrently contact the rising vapors. This process concentrates the volatile components in the overhead stream. Steam may either be directly injected or reboiled, although direct injection is more common. The steam strips volatile pollutants from the wastewater, which are then included in the upward vapor flow. As a result, the wastewater contains progressively lower concentrations of volatile compounds as it moves toward the bottom of the column. The extent of separation is governed by physical properties of the volatile pollutants being stripped, the temperature and pressure at which the column is operated, and the arrangement and type of equipment used.

The difference between steam stripping columns and distillation columns is the location of the feed stream. Stripping columns have a feed stream located near the top of the column while distillation columns have a feed stream located further down the column. Pollutants that phase separate from water can usually be stripped from the wastewater in a steam stripper (a column without rectifying stages). Pollutants that are not phase-separable, such as methanol, need a column with rectifying stages to achieve a high concentration of the pollutants in the overhead stream.

The ancillary equipment used in conjunction with steam stripper and distillation columns includes a condenser and subcooler, pumps for the feed and reflux streams, a feed preheater and bottoms cooler, a decanter, a storage tank, and an air pollution control

device to contain any vapors from the condenser. The condenser and subcooler condense and cool the overhead stream to a temperature amenable for storage and disposal. The pumps supply the force to move the waste stream into the column, either at the feed position or at a point above the feed in the case of a reflux stream. The feed preheater/bottoms cooler is a heat exchanger that heats the feed before it enters the column at the same time it cools the bottoms stream so that it can be sent to a storage area or treatment system. The decanter separates the aqueous layer from the organic layer after the stream comes from the condenser and subcooler. The aqueous layer can be refluxed back to the column while the organic layer is usually disposed of or reused. The storage tank provides a steady feed for the distillation column, equalizing flow and waste variability. An air pollution control device may be needed to contain any pollutants that do not condense in the condenser and would otherwise escape to the air. Wet scrubbers, carbon adsorption devices, or venting to a combustion device may be used to control air emissions. Figure 7-3 shows a flow diagram of a typical steam stripping treatment system and Figure 7-4 shows a flow diagram of a typical distillation treatment system.

The typical construction material for steam stripping and distillation columns in the pharmaceutical manufacturing industry is stainless steel. If a wastewater stream is highly corrosive, a more corrosion-resistant material, such as Hastelloy or Teflon®-lined carbon steel, may be required for construction of the column. The majority of pharmaceutical manufacturing facilities which currently use steam stripping and/or distillation columns to treat their wastewater use stainless steel.

Salts and other pollutants may contribute to scaling and corrosion inside the column. Timely maintenance should be provided to deter scaling problems. Costs of these measures are discussed in Section 10.

The key design parameters for stripping columns are the steam-to-feed ratio and the number of trays or equilibrium stages in packed columns. These parameters are

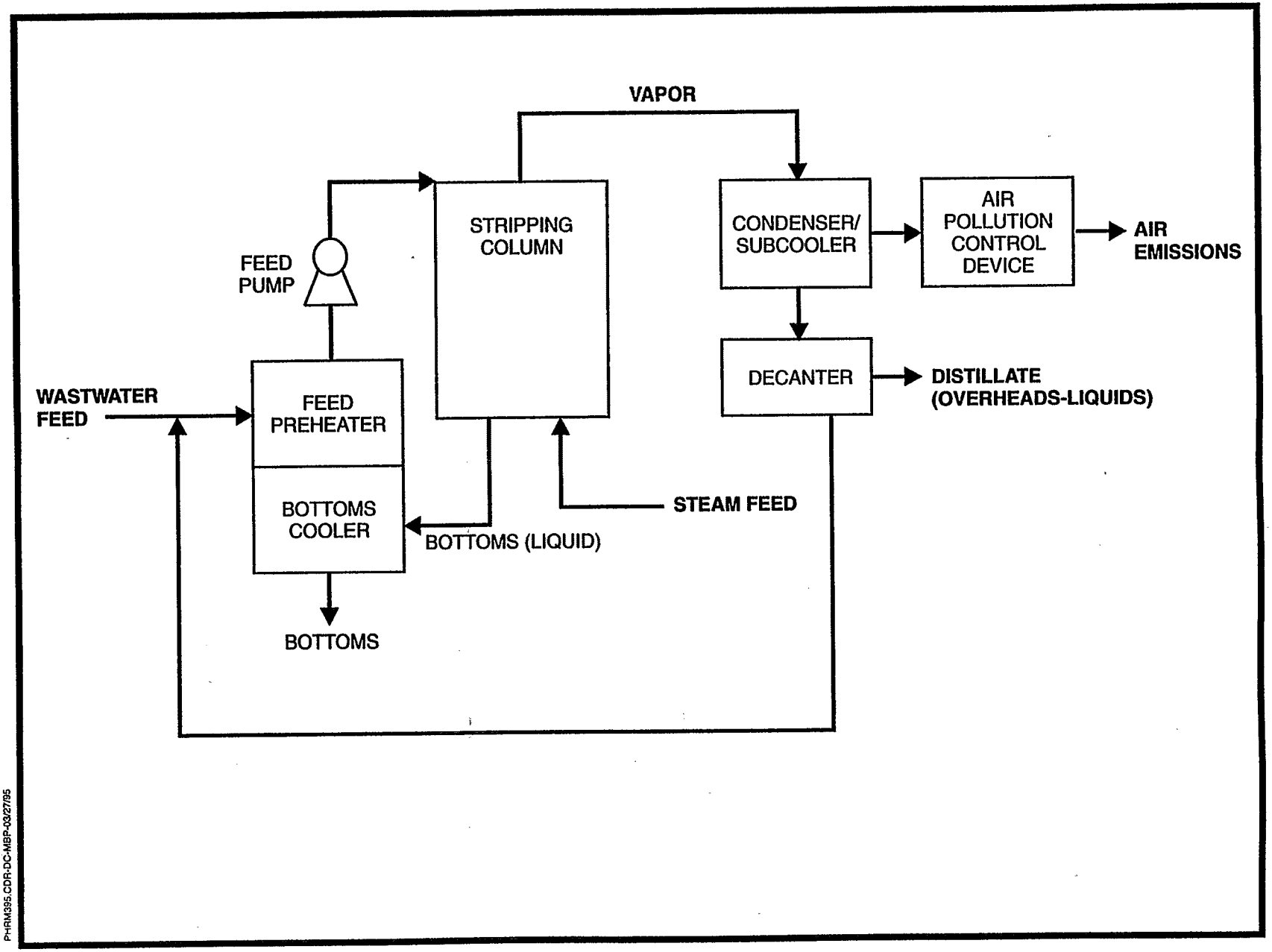

Figure 7-3. Steam Stripping Column Diagram

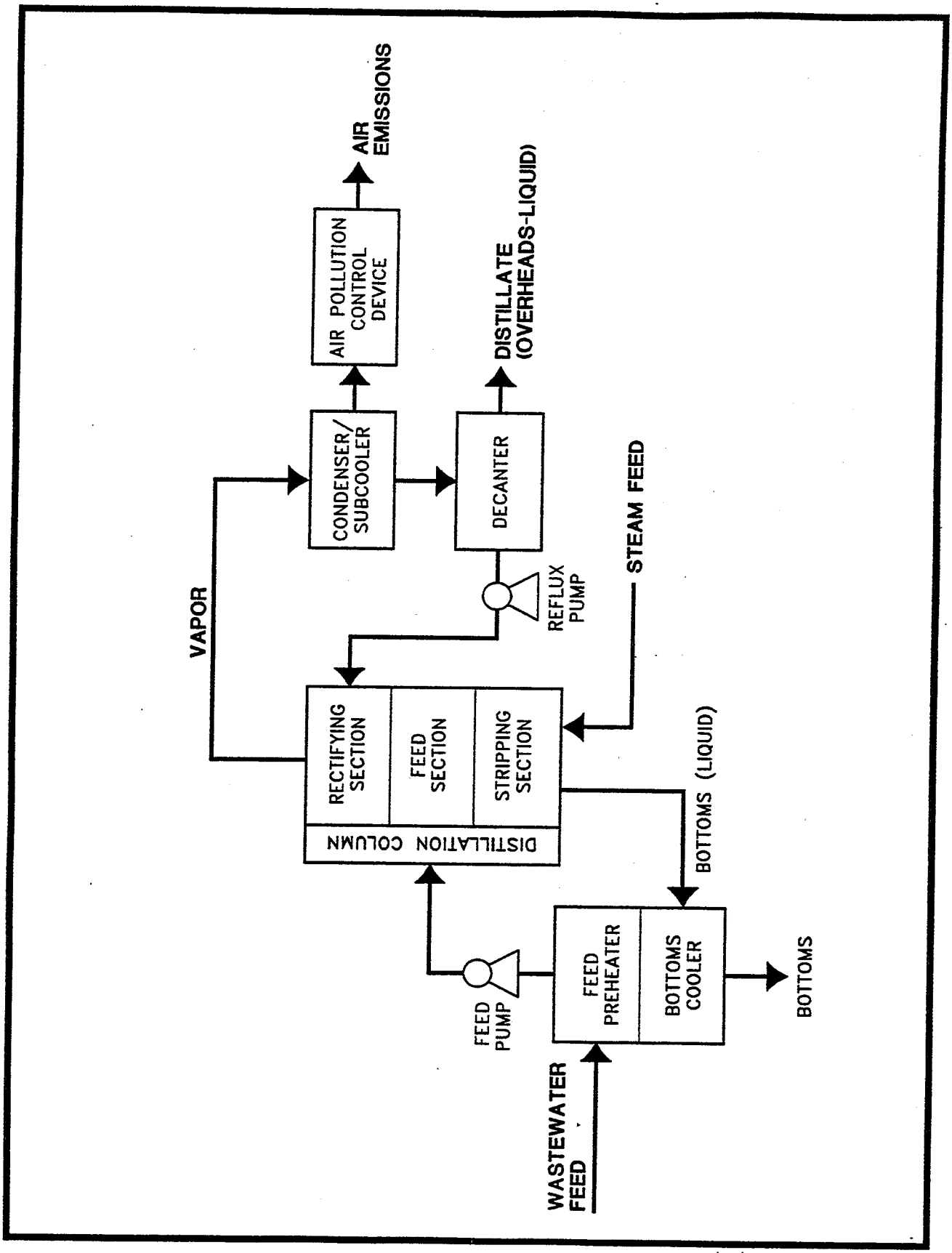

Figure 7-4. Distillation Column Diagram

calculated using the equilibrium ratio of the least strippable contaminant in the wastewater stream and the removal efficiency required to treat the contaminant to the desired concentration. Typical ranges for steam-to-feed ratios vary from 1:3 to 1:35, and the typical number of trays or equilibrium stages vary from 2 to 20. Generally, columns with smaller diameters are packed while columns with larger diameters have trays. Typical column packings are Pall rings, Rashing rings, Berl saddles, and Intalox saddles.

7.2.6.2 Industry Application

In responses to the Detailed Questionnaire, 61 of 244 responding facilities in the pharmaceutical manufacturing industry reported using distillation, distillation with reflux columns, or rectification for solvent recovery operations. Fourteen facilities reported using steam strippers for wastewater treatment. However, a review of these 14 facilities resulted in a determination by the Agency that only four were actually using the technology for wastewater treatment. While the other ten facilities were using the strippers for solvent recovery purposes. Steam stripping and distillation columns are currently used in this industry as stand-alone treatment or as pretreatment before biological treatment. They are also used to recover specific constituents from waste streams. Direct dischargers tend to use steam stripping or distillation as a pretreatment before biological treatment more frequently than as a stand-alone treatment, whereas indirect dischargers tend to use steam stripping or distillation more as a stand-alone treatment or to recover a specific constituent from the waste stream.

7.2.7 Granular Activated Carbon Adsorption

7.2.7.1 General Description

Granular activated carbon (GAC) adsorption is used in the pharmaceutical manufacturing industry to treat BOD_5, COD, or organic constituents in wastewater. Adsorption is a process in which soluble or suspended materials in water are bonded

onto the surface of a solid medium. Activated carbon is an excellent medium for this process because of its high internal surface area, high attraction to most adsorbates (the constituents to be treated), and the fact that it is hydrophobic (water will not occupy bonding sites and interfere with the adsorption process). Constituents in the wastewater bond onto the GAC grains until all surface bonding sites are occupied. At this point, the carbon is considered to be "spent", and requires regeneration, cleaning, or disposal.

Activated carbon is normally produced in two standard grain sizes: powdered activated carbon (PAC) with diameters less than a 200 mesh, and GAC with diameters greater than 0.1 mm. PAC is generally added to the wastewater, whereas GAC is normally used in flow-through fixed bed units.

For treatment units, GAC is packed into one or more beds or columns. Multiple beds are more common, and are normally operated in series because this design allows for monitoring between beds, and therefore minimizes the risk of discharging wastewater from the system with concentrations above acceptable levels. Wastewater flows through a bed and is allowed to come in contact with all portions of the GAC. The GAC in the upper layers of the bed is spent first as bonding sites are occupied, and the GAC in progressively lower regions is spent over time as the adsorption zone moves down through the unit. When contaminant concentrations begin to increase at the bottom of the bed above acceptable levels, the bed is considered to be spent and must be removed. The above description assumes that beds are operated in downflow mode; however, it is also possible to use an upflow design for GAC systems.

Once a bed is spent, the carbon can be treated in three ways: regeneration, backwash, or disposal. Normally, it is possible to use high heat (1,500 to 1,700° F), steam, or chemical treatment to regenerate the spent carbon. These processes remove contaminants from the carbon without significantly affecting the carbon itself; however, some carbon is lost each time this procedure is performed, and carbon performance decreases slightly with each regeneration. Because the bonds formed between the GAC and the adsorbate are

not generally strong, it may also be possible to backwash the carbon bed as described in Section 7.2.3. If the carbon cannot be regenerated or backwashed, it must be disposed of as a solid waste.

The performance of GAC treatment units can be affected by several factors. Three important design criteria are saturation loading, wastewater TSS concentration, and hydraulic loading. Saturation loading is a treatment performance coefficient relating mass of contaminant adsorbed versus mass of carbon used. If this coefficient is very low (as is the case for highly soluble constituents), a GAC system will not perform efficiently. Parameters that effect solubility (i.e., pH and temperature) must also be considered when calculating a design saturation loading for a system. High TSS concentrations in wastewater will foul the GAC system. Solids will occupy bonding sites on the carbon and will get plugged in the pore spaces between GAC grains. If this happens, head loss may occur and a portion of the carbon bed will not be used for treatment. In some cases, it may be necessary to install some type of filtration prior to GAC treatment to keep TSS concentrations within acceptable limits. The amount of time the wastewater spends in contact with the GAC is directly related to hydraulic loading rate. If this time is not long enough, effluent contaminant concentrations will be higher than expected.(2)(3)

7.2.7.2 Industry Application

Based on responses to the Detailed Questionnaire, 10 of 244 responding pharmaceutical manufacturing facilities use GAC treatment to reduce concentrations of organic constituents (and BOD_5 and COD) in wastewater. This treatment is generally used directly after a production area or somewhere prior to the facility treatment plant. GAC treatment can also be used to remove organics following biological treatment.

7.2.8 pH Adjustment/Neutralization

7.2.8.1 General Description

Because many treatment technologies used in the pharmaceutical manufacturing industry are sensitive to pH fluctuations, pH adjustment, or neutralization, may be required as part of an effective treatment system. A pH adjustment system normally consists of a small tank (10 to 30 minutes retention time) with mixing and a chemical addition system. To adjust pH to a desired value, either acids or caustics can be added in the mixing tank. Some treatment technologies require a high or low pH to effectively perform treatment (e.g., air stripping of ammonia requires a pH 10 to 11). pH is generally adjusted to between 6 and 9 prior to final discharge.

7.2.8.2 Industry Application

Based on responses to the Detailed Questionnaire, 126 of 244 responding facilities in the pharmaceutical manufacturing industry use pH adjustment or neutralization treatment of wastes. Retention times for these treatment units average approximately one hour.

7.2.9 Equalization

7.2.9.1 General Description

Because many of the treatment technologies listed in this section are performed continuously and some are sensitive to spikes of high flow or high contaminant concentrations, it is necessary to include equalization as a part of most treatment systems. Equalization is normally performed in large tanks or basins designed to hold a certain percentage of a facility's daily wastewater flow. Equalization will equalize high- and low-flow portions of a typical production day by allowing wastewater to be discharged to downstream treatment operations at a constant flow rate. Equalization can

also provide a continuous wastewater feed to operations such as biological treatment that perform more effectively under continuous load conditions.

The mixing that occurs in an equalization basin minimizes spikes of various contaminants in the discharged wastewater. This equalization will prevent loss of treatment effectiveness or treatment system failures associated with these spikes.

7.2.9.2 Industry Application

Based on responses to the Detailed Questionnaire, 70 of 244 responding facilities in the pharmaceutical manufacturing industry use equalization. Retention times for these treatment units average approximately 20 hours.

7.2.10 Air Stripping

7.2.10.1 General Description

Air stripping is used in the pharmaceutical manufacturing industry to remove volatile organic constituents from wastewater. Air stripping can also be used to remove ammonia from wastewater. Air stripping is normally performed in a countercurrent, packed tower or tray tower column. In these systems, the wastewater is introduced at the top of the column and allowed to flow downward through the packing material or trays. Air is simultaneously delivered at the bottom of the column and blows upward through the water stream. Volatile organics are stripped from the water stream, transferred to the air stream, and carried out of the system at the top of the column. Treated water discharges from the bottom of the column. If ammonia treatment is desired, the pH of the waste stream would be adjusted to between 10 and 11 prior to introduction to the column.

7.2.10.2 Industry Application

Based on responses to the Detailed Questionnaire, 2 of 244 responding pharmaceutical manufacturing facilities use air strippers to treat wastewater. This technology is not common in the industry, and its use has decreased due to increasingly strict air emission regulations. Because the standard air stripper design simply transfers pollutants from water to air, the Agency does not regard it as an acceptable treatment technology and is not proposing air stripping as part of the technology bases for any of the regulatory options.

7.2.11 Incineration

7.2.11.1 General Description

Incineration is used in the pharmaceutical manufacturing industry to treat organic and inorganic constituents in wastewater. This treatment is typically performed in a fixed bed or multiple hearth incinerator equipped with an acid gas scrubber for control of generated hydrochloric acid. Contaminants in the wastewater are destroyed by combustion and the remaining water vapor is discharged to the atmosphere.

7.2.11.2 Industry Application

Based on responses to the Detailed Questionnaire, 12 of 244 responding pharmaceutical manufacturing facilities use incinerators to treat wastewater. Because incineration is costly and energy-intensive when used to treat high-water content streams and does not allow for recycle or reuse of constituents contained in wastewater, the Agency is not proposing incineration as part of the technology bases for any of the regulatory options.

7.3 Development of Control and Treatment Options

7.3.1 Introduction

This section describes the combinations of treatment technologies that the Agency configured as technology options for consideration as bases for the following proposed regulations:

- Best practicable control technology currently available (BPT);
- Best conventional pollutant control technology (BCT);
- Best available technology economically achievable (BAT);
- New source performance standards (NSPS);
- Pretreatment standards for existing sources (PSES); and
- Pretreatment standards for new sources (PSNS).

Treatment technologies for each option are selected from the list of technologies presented in Section 7.2, and include advanced biological treatment, multimedia filtration, polishing pond treatment, cyanide destruction, steam stripping, distillation, and granular activated carbon adsorption.

These proposed regulations would establish limits on the discharge of pollutants from industrial point sources. All of these proposed regulations are based upon the performance of specific technologies, but do not require the use of any specific technology. The proposed regulations applicable to direct dischargers (BPT, BCT, BAT, NSPS) are effluent limitations guidelines and standards that are applied to individual facilities through NPDES permits issued by EPA or authorized states under Section 402 of the CWA. The proposed regulations applicable to indirect dischargers (PSES, PSNS) are standards, and are administered by local permitting authorities (i.e., the government entity controlling the POTW to which the industrial wastewater is discharged). The proposed pretreatment standards are designed to control pollutants that pass through or interfere with POTWs.

The treatment technologies that form the basis of the BPT options were selected to provide reduction of BOD_5, COD, TSS, and cyanide in pharmaceutical manufacturing wastewater. The treatment technologies that form the basis of the BCT options were selected to provide reduction of BOD_5 and TSS beyond the removals of these pollutants achieved by BPT effluent limitations guidelines. The treatment technologies that form the basis of BAT, PSES, NSPS, and PSNS options were selected to provide reduction of organic constituents, ammonia, and cyanide. Section 6 identifies the list of organic constituents proposed to be regulated by these options.

Sections 7.3.2 through 7.3.7 provide discussions of each of the regulatory options described above, including listing treatment technologies that form the basis of each option, and the rationale for the development of each of the options. Technologies included under each regulatory option vary by subcategory and are therefore presented in separate subsections for Subcategories A and C and Subcategories B and D, respectively. Table 7-3 summarizes the regulatory options, identifying the treatment technologies included under each one.

7.3.2 Best Practicable Control Technology Currently Available (BPT)

Effluent limitations guidelines based on the best practicable control technology currently available establish quantitative limits on the direct discharge of pollutants from existing industrial point sources. BPT effluent limitations guidelines are based upon the average of the best existing performance, generally in terms of treated effluent discharged by facilities of various sizes, ages, and unit processes within an industry or subcategory. BPT effluent limitations guidelines are most commonly developed for the control of conventional and nonconventional pollutants, but also may be used for the control of priority pollutants, such as cyanide for this industry.

In developing BPT, the Agency considers the total cost of applying the technology in relation to the effluent reduction benefits to be achieved from the technologies; the size

and age of equipment and facilities; the processes used; the engineering aspects of applying various types of control techniques; process changes; and nonwater quality environmental impacts, including energy requirements.

7.3.2.1 Subcategories A and C

There are five technology options considered as BPT for Subcategories A and C. Option 1 represents the current level of biological treatment and does not represent an upgrade to existing systems. Option 2 consists of an advanced biological treatment (activated sludge) system installed immediately prior to the off-site wastewater discharge point (end-of-pipe), and cyanide treatment with an in-plant hydrogen peroxide cyanide destruction unit (in-plant defined as being immediately downstream of the process area generating the cyanide-bearing wastewater and prior to commingling with any other process or nonprocess wastewaters). As discussed in Section 8, advanced biological treatment provides significant removal of BOD_5, COD, TSS, and ammonia and is widely used in the pharmaceutical manufacturing industry. Cyanide treatment based on in-plant hydrogen peroxide oxidation is part of all BPT options. Cyanide-bearing wastewaters are of concern at certain pharmaceutical manufacturing facilities, and the current regulations for cyanide discharges are based on outdated treatment methods. The hydrogen peroxide cyanide treatment method was selected because it has displayed comparable or superior performance to other cyanide treatment technologies currently used in the pharmaceutical manufacturing industry. Options 3, 4 and 5 provide the same level of BOD_5, COD, and cyanide treatment as Option 2, while progressively increasing the level of TSS treatment. Option 3 combines the same treatment technologies as Option 2, and adds multimedia filtration downstream of the biological treatment unit. Option 4 combines the same treatment technologies as Option 2, and adds polishing pond treatment downstream of the biological treatment unit. Option 5 includes both multimedia filtration and polishing pond treatment, in that order, following biological treatment.

7.3.2.2 Subcategories B and D

Three BPT options are considered for Subcategories B and D. Option 1 represents the current level of biological treatment and does not represent an upgrade to existing systems. Option 2 consists of advanced biological treatment. Option 3 provides the same level of treatment for BOD_5 and COD, and adds improved TSS treatment by adding a multimedia filtration unit downstream of the biological treatment unit. None of the BPT options for Subcategories B and D include cyanide treatment technology. This is because EPA has determined that cyanide is neither used nor generated by facilities with Subcategory B and/or D operations. Accordingly, EPA proposes to repeal the existing BPT limitations for Subcategories B and D pertaining to cyanide.

7.3.2.3 Rationale

Advanced biological treatment is the basic treatment in each of the technology options described above. Biological treatment is a well-established method for treating BOD_5 and COD in wastewater and is the most common method in the pharmaceutical manufacturing industry for treating BOD_5. Of the facilities in the industry that reported using biological treatment, 74% use the activated sludge process. Biological treatment systems, including activated sludge systems, can be operated in nitrifying mode, thereby achieving significant ammonia removal. The secondary clarifier, which is a standard component of the biological treatment system, provides TSS treatment of the wastewater prior to discharge from the system.

Because cyanide and ammonia are not present at concentrations of concern in Subcategory B and D wastewaters, cyanide destruction and ammonia treatment technologies are not included under the Subcategory B and D options.

Multimedia filtration is an established technology for treating TSS in wastewater. For Subcategories B and D, this TSS treatment technology is included under a separate option to fully evaluate the cost-effectiveness associated with this alternative.

The treatment performance of each of the options described above is discussed in Section 8.

7.3.3 Best Conventional Pollutant Control Technology (BCT)

Effluent limitations guidelines based on the best conventional pollutant control technology establish quantitative limits on the direct discharge of conventional pollutants from existing industrial point sources. In contrast to BPT guidelines that are devised as the average of the best existing performance by a group of like facilities, BCT guidelines are developed by identifying candidate technologies and evaluating their cost-reasonableness. Effluent limitations guidelines based upon BCT may not be less stringent than BPT effluent limitations guidelines. As such, BPT effluent limitations are a "floor" below which BCT efficient limitations guidelines cannot be established. EPA has developed a BCT cost test methodology to assist the Agency in determining whether it is "cost-reasonable" for industry to control conventional pollutants at a level more stringent than would be required by BPT effluent limitations. This methodology is fully described in Section 14.

In performing the BCT cost test, a BPT baseline must be developed to serve as the starting point against which more stringent technologies are analyzed. In each subcategory, EPA conducted the BCT analysis assuming the baseline was BPT Option 2 (i.e., advanced biological treatment).

7.3.3.1 Subcategories A and C

The five BCT treatment options for Subcategories A and C are the same as the BPT options for Subcategories A and C presented in the previous section, with the exception of cyanide treatment, which is not included under BCT because cyanide is not a conventional pollutant. COD, a nonconventional pollutant, is also omitted because BCT controls conventional pollutants only.

7.3.3.2 Subcategories B and D

The three BCT treatment options for Subcategories B and D are the same as the BPT options for Subcategories B and D presented in the previous section, except that the BCT treatment options do not address COD.

7.3.3.3 Rationale

The rationale for the treatment technologies included under BCT is the same as that presented for BPT (omitting references to cyanide and COD, which are not included under BCT).

7.3.4 Best Available Technology Economically Achievable (BAT)

Effluent limitations guidelines based on the best available technology economically achievable establish quantitative limits on the direct discharge of priority and nonconventional pollutants to waters of the United States. These limits are based upon the performance of specific technologies, but they do not require the use of any specific technology. BAT effluent limitations guidelines are applied to individual facilities through NPDES permits issued by EPA or authorized states under Section 402 of the CWA. The facility then chooses its own approach to complying with its permit limitations.

The technology selected by the Agency to define the BAT performance may include end-of-pipe treatment, process changes, and internal controls, even when these technologies are not common industry practice. BAT performance is established for groups of facilities with shared characteristics. Where a group of facilities demonstrates uniformly inadequate performance in controlling pollutants of concern, BAT may be transferred from a different subcategory or industrial category.

A primary consideration in selecting BAT is the effluent pollutant reduction capability of the available technologies. Implementation of the best available technology must be economically achievable by the industry, so the cost of applying the technology is also considered. Other factors considered in establishing BAT include:

- The processes used;
- Engineering aspects of the application of various types of control techniques;
- Potential process changes;
- Age and size of equipment and facilities; and
- Nonwater quality environmental impacts, including energy requirements.

7.3.4.1 Subcategories A and C

Four BAT technology options were considered for Subcategories A and C. Option 1 provides treatment of ammonia and the organic priority and nonconventional pollutants of concern based on an end-of-pipe advanced biological treatment (activated sludge) system and cyanide treatment with an in-plant hydrogen peroxide cyanide destruction unit (in-plant defined as being immediately downstream of the process area generating the cyanide-bearing wastewater and prior to commingling with any other process or nonprocess wastewaters). As discussed in Section 8, advanced biological treatment

provides treatment of organic pollutants, and is widely used in the pharmaceutical manufacturing industry. Cyanide treatment based on in-plant hydrogen peroxide oxidation is provided as part of all BAT options because the current regulations for cyanide discharges are based on outdated treatment methods. The hydrogen peroxide cyanide treatment method was selected because it has displayed comparable or superior performance compared to other treatment technologies currently used in the pharmaceutical manufacturing industry.

Option 2 includes all of the treatment technologies from Option 1, and provides increased treatment of organic constituents by adding in-plant steam stripping. In-plant steam stripping consists of steam stripper columns placed prior to dilution by non-process wastewater, commingling with other treated wastestreams, and any equalization or treatment units that are open to the atmosphere. This treatment is included for all process area wastewaters that contain strippable pollutants at concentrations above the performance levels achieved by steam stripping.

Option 3 includes all of the treatment technologies from Option 2, and provides increased treatment of organic constituents by using distillation columns for harder to strip, soluble organics such as alcohols and ketones. The use of distillation columns with rectifying stages allows steam rates to be increased without causing a significant increase in waste overhead organic material, because the organic material is concentrated in the rectifying section. The increased steam rates result in lower wastewater discharge concentrations of organics in wastewater from the distillation columns. Under Option 3, steam stripping is still used for easy to strip, insoluble organic constituents such as chloroform, methylene chloride, and toluene. The use of steam stripping and distillation technology under Option 3, depending on waste stream characteristics, is referred to throughout the remainder of the development document, and in the preamble to the regulation, as "steam stripping with distillation." Steam stripping with distillation consists of steam stripping or distillation columns placed prior to dilution by non-process wastewater, commingling with other treated wastestreams, and any equalization or

treatment units which are open to the atmosphere. This treatment is included for all process area wastestreams that contain strippable pollutants at concentrations above the performance levels achieved by steam stripping with distillation. Throughout this development document, when reference is made to a specific piece of equipment, or data for a specific piece of equipment, the terms "steam stripping" and "distillation" are used to describe the equipment as appropriate.

Option 4 includes all of the technologies from Option 3, and provides increased treatment of COD and specific organic constituents by adding granular activated carbon adsorption treatment downstream of the advanced biological treatment unit.

7.3.4.2 Subcategories B and D

BAT technology options for Subcategories B and D are the same as BAT options for Subcategories A and C, with the exception that cyanide destruction is not included.

7.3.4.3 Rationale

Advanced biological treatment is the basic treatment operation in each of the technology options described above. Biological treatment is a proven method for treating organic constituents in pharmaceutical manufacturing industry wastewater. Treatment performance data for advanced biological treatment and the other technologies included in the BAT options are provided in Section 8. Of the facilities in the industry that reported using biological treatment, 74% use the activated sludge process. Biological treatment systems, including activated sludge systems, can be operated in nitrifying mode, thereby achieving significant ammonia removal. Options 2 and 3 include the same technology as Option 1 with addition of in-plant steam stripping or steam stripping with distillation. In-plant steam stripping or steam stripping with distillation offers the following benefits:

- Minimizes cross-media impacts by capturing pollutants that might escape to the air during handling and biological treatment of wastewater;

- Increases the pollution prevention opportunities for a facility by allowing recycle and reuse of recovered solvents;

- Is more flexible than biological treatment in that discontinuation of flow and spikes of higher pollutant concentrations are accepted more easily by the system; and

- Provides treatment of some constituents that are not amenable to biological treatment in addition to incidental removal of ammonia.

The steam stripping with distillation component of Option 3 offers greater pollutant reduction benefits than the steam stripping component of Option 2, but uses more steam and as a result has a greater energy consumption impact.

Option 4 provides additional treatment of organics by adding GAC units. GAC treatment is a widely used polishing technique for removing organics from wastewater prior to discharge.

Because cyanide and ammonia are not present at concentrations of concern in Subcategory B and D wastewaters, cyanide destruction and ammonia treatment are not included under the Subcategory B and D options.

7.3.5 New Source Performance Standards (NSPS)

The basis for new source performance standards under Section 306 of the CWA is the best available demonstrated technology. Industry has the opportunity to design and install the best and most efficient processes and wastewater treatment facilities at new facilities. Accordingly, Congress directed EPA to consider the best demonstrated alternative processes, process changes, in-plant control measures, and end-of-pipe wastewater treatment technologies that reduce pollution to the maximum extent feasible.

In response to that directive, and as with the development of options for the proposed BAT effluent limitations guidelines, EPA considered effluent reductions attainable by the most advanced and demonstrated process and treatment technologies at pharmaceutical manufacturing facilities.

7.3.5.1 Subcategories A and C

Two NSPS options were developed for Subcategories A and C. Option 1 consists of cyanide treatment by an in-plant hydrogen peroxide cyanide destruction unit, in-plant steam stripping with distillation for treatment of organic pollutants (and ammonia), and an end-of-pipe advanced biological treatment (activated sludge) system. Option 2 includes the technologies from Option 1, and adds increased treatment of COD and specific organic constituents by adding a granular activated carbon adsorption treatment unit directly downstream of the biological treatment unit.

7.3.5.2 Subcategories B and D

NSPS technology options for Subcategories B and D are the same as NSPS options for Subcategories A and C, with the exception that cyanide destruction is not included.

7.3.5.3 Rationale

Because new plants have the opportunity to install the best and most efficient wastewater treatment technologies, NSPS should be based on the most stringent control technology demonstrated for all pollutants of concern (conventional, nonconventional, and priority pollutants). The two NSPS options include the most advanced wastewater treatment technologies demonstrated to effectively treat pharmaceutical manufacturing industry wastewater. The NSPS options address the treatment of conventional, nonconventional, and priority pollutants in Subcategory A and/or C and Subcategory B and/or D wastewaters. Because cyanide and ammonia are not present in wastewaters at

concentrations of concern at existing Subcategory B and D facilities, cyanide destruction and ammonia treatments are not included under the NSPS options for Subcategories B and D.

7.3.6 Pretreatment Standards for Existing Sources (PSES)

Pretreatment standards for existing sources establish quantitative limits on the indirect discharge of priority and nonconventional pollutants to waters of the United States (i.e.) PSES limit industrial discharges to POTWs. PSES are designed to prevent the discharge of pollutants which pass through, interfere with, or are otherwise incompatible with the operation of POTWs. The CWA requires pretreatment for pollutants that pass through POTWs in amounts that would exceed direct discharge effluent limitations or limit POTW sludge management alternatives, including the beneficial use of sludges on agricultural lands. Pretreatment standards are to be technology-based and analogous to BAT for removal of priority and nonconventional pollutants. Like effluent guidelines limitations and standards based on BPT, BCT, BAT, and NSPS, PSES do not require the use of any specific technology.

7.3.6.1 Subcategories A and C

Four PSES technology options were considered for Subcategories A and C. Option 1 provides treatment of organic constituents (and ammonia) by in-plant steam stripping, and treatment of cyanide by an in-plant hydrogen peroxide cyanide destruction system. Option 2 provides treatment of organic constituents (and ammonia) by in-plant steam stripping with distillation, and treatment of cyanide by an in-plant hydrogen peroxide cyanide destruction system. Option 3 includes the technologies from Option 2 and provides additional treatment of organics by adding an end-of-pipe advanced biological treatment (activated sludge) system. Option 4 includes the technologies from Option 3 with additional treatment of COD and specific organic constituents by adding a granular activated carbon adsorption system downstream of the biological treatment system.

7.3.6.2 Subcategories B and D

Three treatment options are included under PSES for Subcategories B and D. Option 1 consists of in-plant steam stripping for treatment of organic constituents. Option 2 consists of in-plant steam stripping with distillation for treatment of organic constituents. Option 3 combines in-plant steam stripping with distillation with subsequent granular activated carbon adsorption treatment for increased reduction of COD and specific organic constituents in wastewater.

7.3.6.3 Rationale

In-plant steam stripping and steam stripping with distillation are effective techniques for the removal of priority and nonconventional pollutants of concern in pharmaceutical manufacturing wastewater. Steam stripping and steam stripping with distillation provide effective pretreatment of wastewater that is further treated off site by biological treatment at a POTW. Of the 53 pollutants in pharmaceutical manufacturing wastewater that have been identified to pass through or interfere with POTWs, pretreatment by steam stripping or steam stripping with distillation eliminates the pass-through problem for 48 pollutants (the other five pollutants are not amenable to treatment by steam stripping or steam stripping with distillation). With Option 3, the Agency has also evaluated the addition of end-of-pipe advanced biological treatment for Subcategory A and C indirect dischargers to provide additional treatment of organics that are not amenable to steam stripping and distillation. As discussed previously, granular activated carbon is an effective treatment process for reducing concentrations of COD and specific organic constituents in wastewater, especially when used as a polishing step after other treatment technologies. This technology is added in Option 4.

Cyanide and ammonia are not present at concentrations of concern in Subcategory B and D wastewaters; therefore, cyanide destruction and ammonia treatment are not included under the Subcategory B and D options. Additionally, because loadings are

much smaller at Subcategory B and D indirect dischargers (averaging 14,586 pounds per facility) as compared to Subcategory A and C indirect dischargers (averaging 377,246 pounds per facility), it was determined that biological treatment beyond what is currently provided at the POTW would not be appropriate treatment of wastewater from Subcategory B and D facilities. Therefore, all proposed options for Subcategories B and D include in-plant steam stripping or steam stripping with distillation without any end-of-pipe biological treatment.

7.3.7 Pretreatment Standards for New Sources (PSNS)

Pretreatment standards for new sources establish quantitative limits on the indirect discharge of priority and nonconventional pollutants to waters of the United States. Section 307(c) of the CWA requires EPA to promulgate PSNS at the same time it promulgates NSPS. New indirect dischargers, like new direct dischargers, have the opportunity to incorporate the best available demonstrated technologies, including process changes, in-plant controls, and end-of-pipe treatment technologies.

As discussed in Section 17, EPA determined that a broad range of priority and nonconventional organic pollutants, ammonia, and cyanide pass through POTWs. PSNS are applicable to these pollutants.

7.3.7.1 Subcategories A and C

EPA considered three PSNS technology options for Subcategories A and C. Option 1 consists of in-plant steam stripping with distillation for treatment of organics and ammonia. Option 2 consists of in-plant distillation and end-of-pipe advanced biological treatment (activated sludge) for treatment of organics and ammonia. Treatment of cyanide is based on an in-plant hydrogen peroxide cyanide destruction unit for both of these options. Option 3 includes Option 2 treatment technologies and provides

additional treatment of COD and specific organic constituents by adding granular activated carbon adsorption treatment downstream of the biological treatment system.

7.3.7.2 Subcategories B and D

EPA considered two options under PSNS for Subcategories B and D. Option 1 consists of in-plant steam stripping with distillation for treatment of organic constituents. Option 2 combines in-plant steam stripping with distillation with granular activated carbon adsorption treatment for increased reduction of COD and specific organic constituents. EPA did not consider a technology option employing advanced biological treatment for the same reasons EPA rejected end-of-pipe advanced biological treatment as part of the PSES technology options.

7.3.7.3 Rationale

New indirect dischargers, like new direct dischargers, have the opportunity to incorporate into their plants the best available wastewater treatment technologies. Therefore, the treatment technologies included in the PSNS options are the most advanced wastewater treatment technologies demonstrated to effectively treat pharmaceutical manufacturing industry wastewater. The PSNS technology options address the treatment of organics, ammonia, and cyanide in Subcategory A and C wastewater and organics in Subcategory B and D wastewater. Since cyanide and ammonia are not present in wastewater at concentrations of concern at Subcategory B and D facilities, cyanide destruction and ammonia treatment are not included under the Subcategory B and D options.

Table 7-1

Summary of Major Treatment Technologies Used in the Pharmaceutical Manufacturing Industry

Technology	Number of Facilities Using the Technology(a)	
	Subcategory A and C	Subcategory B and D
pH Adjustment/Neutralization	81	45
Equalization	44	26
Biological Treatment		
Single-Stage Activated Sludge	31	21
Two-Stage Activated Sludge	2	2
Oxygen Activated Sludge	1	1
Aerated Lagoons	7	5
Trickling Filters	4	1
Rotating Biological Contactors	2	1
Multimedia Filtration	3	3
Cyanide Destruction		
Alkaline Chlorination	6	0
H_2O_2 Oxidation	3	0
Hydrolysis	1	0
Distillation Technologies		
Solvent Recovery		
Distillation	12	3
Distillation with reflux	28	5
Rectification	12	1
Wastewater treatment		
Steam stripping	4 (b)	0
Carbon Adsorption	6	4
Polishing Pond	2	6
Air Stripping	2	0
Incineration	10	1

(a)Data based on responses from the Detailed Questionnaire (244 responding facilities).
(b)In their Detailed Questionnaire responses, 14 facilities reported using steam stripping for wastewater treatment; however, based on a review of each of these facilities, EPA determined that only four facilities were actually using the technology for wastewater treatment.

Table 7-2

Pharmaceutical Manufacturing Facilities
Quantity of Chemicals Recycled/Reused (1990)

Chemical Name	Number of Facilities Reporting	Total Quantity Recycled/Reused (lbs)
Acetone	2	17,107,958
Acetonitrile	2	10,518,000
n-Butyl acetate	1	37,302,726
1,2-Dichloroethane	2	187,020
Ethyl acetate	1	10,243,000
Ethyl alcohol	1	122,304,000
Heptane	1	5,680,400
Hexane	1	248,082
Isopropanol	1	27,441
Methanol	7	19,027,784
Methylene chloride	7	92,599,587
Pyridine	1	451,000
Tetrahydrofuran	1	76,666
Toluene	6	19,185,893
Triethylamine	1	29,534
TOTAL		334,989,091

Table 7-3

Summary of Regulatory Options

Regulation		Subcategory A and C Facilities	Subcategory B and D Facilities
BPT	Option 1	Current Biological Treatment	Current Biological Treatment
	Option 2	In-plant Cyanide Destruction + Advanced Biological Treatment	Advanced Biological Treatment
	Option 3	In-plant Cyanide Destruction + Advanced Biological Treatment + Effluent Filtration	Advanced Biological Treatment + Effluent Filtration
	Option 4	In-plant Cyanide Destruction + Advanced Biological Treatment + Polishing Pond	None
	Option 5	In-plant Cyanide Destruction + Advanced Biological Treatment + Effluent Filtration + Polishing Pond	None
BCT	Option 1	Current Biological Treatment	Current Biological Treatment
	Option 2	Advanced Biological Treatment	Advanced Biological Treatment
	Option 3	Advanced Biological Treatment + Effluent Filtration	Advanced Biological Treatment + Effluent Filtration
	Option 4	Advanced Biological Treatment + Polishing Pond	None
	Option 5	Advanced Biological Treatment + Effluent Filtration + Polishing Pond	None
BAT	Option 1	In-Plant Cyanide Destruction + Advanced Biological Treatment With Nitrification	Advanced Biological Treatment
	Option 2	In-Plant Steam Stripping + In-Plant Cyanide Destruction + Advanced Biological Treatment	In-Plant Steam Stripping + Advanced Biological Treatment
	Option 3	In-Plant Steam Stripping with Distillation + In-plant Cyanide Destruction + Advanced Biological Treatment	In-Plant Steam Stripping with Distillation + Advanced Biological Treatment
	Option 4	In-Plant Steam Stripping with Distillation + In-plant Cyanide Destruction + Advanced Biological Treatment + Granular Activated Carbon Adsorption	In-Plant Steam Stripping with Distillation + Advanced Biological Treatment + Granular Activated Carbon Adsorption

Table 7-3

(Continued)

Regulation		Subcategory A and C Facilities	Subcategory B and D Facilities
NSPS	Option 1	In-Plant Steam Stripping with Distillation + In-plant Cyanide Destruction + Advanced Biological Treatment	In-Plant Steam Stripping with Distillation + Advanced Biological Treatment
	Option 2	In-Plant Steam Stripping with Distillation + In-plant Cyanide Destruction + Advanced Biological Treatment + Granular Activated Carbon Adsorption	In-Plant Steam Stripping with Distillation + Advanced Biological Treatment + Granular Activated Carbon Adsorption
PSES	Option 1	In-Plant Steam Stripping + In-Plant Cyanide Destruction	In-Plant Steam Stripping
	Option 2	In-Plant Steam Stripping with Distillation + In-plant Cyanide Destruction	In-Plant Steam Stripping with Distillation
	Option 3	In-Plant Steam Stripping with Distillation + In-plant Cyanide Destruction + Advanced Biological Treatment	In-Plant Steam Stripping with Distillation + Granular Activated Carbon Adsorption
	Option 4	In-Plant Steam Stripping with Distillation + In-plant Cyanide Destruction + Advanced Biological Treatment + Granular Activated Carbon Adsorption	None
PSNS	Option 1	In-Plant Steam Stripping with Distillation + In-plant Cyanide Destruction	In-Plant Steam Stripping with Distillation
	Option 2	In-Plant Steam Stripping with Distillation + In-plant Cyanide Destruction + Advanced Biological Treatment	In-Plant Steam Stripping with Distillation + Granular Activated Carbon Adsorption
	Option 3	In-Plant Steam Stripping with Distillation + In-plant Cyanide Destruction + Advanced Biological Treatment + Granular Activated Carbon Adsorption	None

REFERENCES

1. U.S. EPA, Washington, D.C. Facility Pollution Prevention Guide, May 1992.

2. U.S. EPA, Office of Solid Waste. Treatment Technology Background Document, January 1991.

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4. U.S. EPA, Office of Water. Development Document for Effluent Limitations Guidelines and Standards for the Aluminum Forming Point Source Category. EPA 440/1-84/073, U.S. Environmental Protection Agency, Washington, D.C., June 1984.

SECTION 8

PERFORMANCE OF THE CONTROL AND TREATMENT OPTIONS

8.1 Introduction

This section discusses the treatment performance data collected and available to the Agency for the treatment technologies discussed in Section 7 and for the constituents and pollutant parameters proposed for regulation in Section 6. The subsections below list, by technology, criteria applied to available datasets to determine which data corresponded to well-designed/well-operated treatment units that could be used in developing long-term mean (LTM) performance levels. Those data meeting the criteria are presented in this section.

The following information is presented in this section:

- Section 8.2 provides an overview of the treatment performance databases developed by the Agency and their sources.
- Section 8.3 provides a technology-by-technology evaluation of treatment performance data, lists the criteria used to identify data associated with well-designed/well-operated systems, and summarizes those datasets that meet the well-designed/well-operated criteria.
- Section 8.4 presents the Agency's rationale for the data transfers developed for this regulation, including process simulation modelling conducted by EPA to support transfers.
- Section 8.5 discusses the development of LTMs for conventional pollutants and COD.
- Section 8.6 discusses the development of the LTM for cyanide.

- Section 8.7 discusses the development of LTMs for priority and nonconventional pollutants.
- Section 8.8 discusses the development of the LTM for ammonia.

8.2 Treatment Performance Databases

There are four main sources of treatment performance data available to the Agency: EPA sampling data; industry-supplied self-monitoring data; data gathered from EPA-sponsored treatability studies; and data collected as part of other research efforts. These sources are described in detail in Section 3.1. The treatment performance data used from these sources are discussed in greater detail below.

8.2.1 EPA Pharmaceutical Manufacturers Sampling Program Data

Beginning in 1978, EPA conducted the Screening and Verification Sampling Programs. Under these programs, wastewater samples were collected from plants with manufacturing operations representative of the pharmaceutical manufacturing industry. In the screening program, in-plant and end-of-pipe wastewater samples from 26 plants were screened for the presence of 129 priority pollutants. Typical sample collection periods were 24 hours during the screening phase. The Agency conducted follow-up sampling (referred to as the verification phase) at five facilities to verify the presence, levels, frequency of discharge, and treatability of the pollutants detected during the screening program. The typical verification sampling program was three days in length.

Between 1983 and 1991, EPA also conducted 15 different sampling episodes at 13 pharmaceutical manufacturing facilities. Data were collected for all pollutants on the List of Analytes during these sampling efforts. These data were used to characterize the pollutants in the wastewater discharged by direct and indirect facilities, to generate

pollutant treatment system performance data from facilities with well-operated biological treatment systems, and to obtain treatability data for steam stripping columns.

The treatment performance data collected from these sampling episodes were incorporated into a sampling database. These data were evaluated against the criteria defined in Section 8.3 to establish data representative of well-designed/well-operated steam stripping, and biological treatment systems for priority and nonconventional pollutants.

8.2.2 Industry-Supplied Self-Monitoring Data

Self-monitoring data were supplied by pharmaceutical manufacturers to the Agency as part of their response to the Detailed Questionnaire (self-monitoring data were also submitted by the seven facilities that participated in the 1989 pretest questionnaire). In addition, the Agency requested self-monitoring data from Facility 30542 on the performance of their cyanide destruction unit, which employs in-plant hydrogen peroxide oxidation treatment. All self-monitoring treatment performance data were evaluated against the criteria defined in Section 8.3 to establish data representative of well-designed/well-operated treatment units. Those data that conformed to the criteria were placed into the Self-Monitoring Database. This database includes biological treatment performance data for conventional, priority, and nonconventional pollutants as well as cyanide treatment performance data.

Self-monitoring data collected during 1982 and 1983 that represent the performance of tertiary multimedia filtration at Subcategory B and D facilities are also available. These data were collected and presented as part of the October 27, 1983 NSPS proposed rule (48 FR 49808) for the pharmaceutical manufacturing industry.

8.2.3 EPA Treatability Studies Data

In 1984, the Agency collected granular activated carbon treatability data for total COD. The data collected as part of this treatability study were evaluated to establish data representing well-designed/well-operated GAC treatment for COD.

In late 1991, the Agency collected steam stripping treatability data for several volatile organic pollutants generated at a pharmaceutical manufacturing facility using a pilot-scale and bench-scale steam stripper. Additionally, the Agency collected distillation treatability data in September of 1993 for methanol, using an existing full-scale distillation column in operation at a pharmaceutical manufacturing facility. The data collected as part of these treatability studies were evaluated against the criteria defined in Section 8.3 to identify data representative of well-designed/well-operated steam stripping and distillation treatment for priority and nonconventional pollutants.

8.2.4 Other Research Sources

In 1979, the Robert S. Kerr Environmental Research Laboratory at Ada, Oklahoma conducted an applied research study to determine the fate of specific priority pollutants within a biological treatment system.(1) In the course of the study, priority pollutants associated with the manufacture of pharmaceuticals were identified at two industrial facilities. The data collected as part of this study were evaluated against the criteria defined in Section 8.3 to identify data representative of well-designed/well-operated biological treatment for priority pollutants.

8.3 Evaluation of Treatment Performance Data

This subsection presents the criteria used to evaluate well-designed/well-operated performance for each technology. The treatment performance data that meet these editing criteria are also presented below.

8.3.1 Advanced Biological Treatment

The Agency has defined "advanced" biological treatment at pharmaceutical manufacturing facilities as those with better than existing BPT-level performance in the industry for treating BOD_5 and COD and as treatment systems that can reduce ammonia in the wastewater through nitrification, where necessary. Advanced biological treatment performance was defined in Section 7.2.2.1 as systems that consistently surpass, on a long-term basis, 90% BOD_5 reduction and 74% COD reduction in pharmaceutical manufacturing wastewater, as required by the existing BPT effluent limitations guidelines (40 CFR Part 439).

These reductions in BOD_5 and COD represent the initial criteria used to identify best performer datasets for advanced biological treatment. For BOD_5, COD, and TSS, an additional criteria established for best performer datasets was that the treatment system represented by the data treat a major portion (49% or more by volume) of pharmaceutical process wastewater in relation to other wastewaters treated by the system.

Table 8-1 presents the BOD_5, COD, and TSS datasets that meet the criteria listed above for best performance. A review of these datasets shows that each is consistently achieving far greater reductions in BOD_5, COD, and TSS discharges than the other plants subject to the existing BPT regulations. Facilities 50002, 50003, 50004, 50005, and 50007 represent best treatment performance for conventional pollutants and COD for Subcategory A and C facilities. Facilities 50008 and 50011 represent best treatment performance for conventional pollutants and COD for Subcategory B and D facilities.

For the identification of applicable datasets for organic pollutants, the percent process wastewater treated criteria was modified to include datasets from treatment systems where pharmaceutical manufacturing wastewater is the predominant wastewater discharged to the treatment system (i.e., including all wastewater from the

pharmaceutical manufacturing area of the facility, not just wastewater from pharmaceutical manufacturing operations.) Additional review criteria included:

- A search of datasets for those constituents and pollutant parameters selected for regulation;
- A review of datasets to ensure that they are representative of advanced biological treatment technology (e.g., datasets representing biological treatment plus powdered activated carbon adsorption were removed from consideration);
- An exclusion of data from facilities that supplied influent data only; and
- A requirement that only data from facilities where the average influent pollutant concentration was at least 10 times greater than the analytical detection limit so that treatment being achieved could be measured.

Table 8-2 presents the organic constituent datasets that meet the criteria listed above for best performance. For organic constituents, treatment performance data from facilities with operations in all subcategories were considered together since the treatment performance data do not demonstrate a difference in treatment based on subcategory. These data are considered representative of treatment performance for all subcategories.

Best performance data for ammonia based on a nitrifying biological treatment system are presented below.

Facility	Pollutant	Influent Conc. (mg/L)			Effluent Conc. (mg/L)			# of Data Points	Source
		Min.	Max.	Avg.	Min.	Max.	Avg.		
30540	Ammonia (aqueous)	25.0	46.3	42.6	1.4	3.7	2.5	9	I

I - EPA (List of Analytes) Sampling Program, Reference 3.

8.3.2 Multimedia Filtration

The Agency has obtained industry-supplied self-monitoring treatment performance data for tertiary filtration from one Subcategory A and C pharmaceutical manufacturing facility (Facility 50007) and from two Subcategory B and D pharmaceutical manufacturing facilities (Facilities 12053 and 12317). TSS reductions through treatment were calculated using these data; datasets that did not include influent concentrations were not included in the calculations. Table 8-3 presents the data that describe the treatment performance of these tertiary filters.

8.3.3 Polishing Ponds

The Agency has obtained industry-supplied self-monitoring treatment performance data describing polishing pond treatment from one Subcategory A and C pharmaceutical manufacturing facility. TSS reductions through treatment were calculated using these data. The calculated reductions were used in developing the TSS LTM representing polishing pond treatment. The table below presents this polishing pond treatment performance data.

Facility	Pollutant	Influent Conc. (mg/L)			Effluent Conc. (mg/L)			# of Data Points	Source
		Min.	Max.	Avg.	Min.	Max.	Avg.		
50007	TSS	4.0	158.0	30.4	4.0	110.0	24.2	462	SMD

SMD - Self-Monitoring Database, Reference 2.

8.3.4 Cyanide Destruction

The Agency requested cyanide destruction data in the Detailed Questionnaire. Ten facilities reported using cyanide destruction systems, including the following types of treatment: hydrogen peroxide oxidation, alkaline chlorination, and hydrolysis. As

discussed in Section 3.1.4, EPA requested Facility 30542 to develop a long-term database documenting the performance of their hydrogen peroxide oxidation cyanide destruction unit. The facility submitted six months of data to EPA in November 1991. EPA also sampled the cyanide destruction unit of this facility during an on-site sample episode.

EPA considered all of the individual datasets representative of the various cyanide destruction technologies in use. The dataset that represents the performance of hydrogen peroxide oxidation technology run in batch mode with analytical sampling of each treated batch to ensure a treated cyanide concentration ≤ 1.0 mg/L achieved significantly greater and more consistent cyanide reduction than that achieved by any of the other technologies. Consequently, EPA is proposing hydrogen peroxide oxidation with batch sampling to ensure treatment concentrations to below 1.0 mg/L prior to discharge (using U.S. EPA Method 335.2) as the technology basis for cyanide destruction in the pharmaceutical manufacturing industry. The self-monitoring data submitted by facility 30542 along with EPA-collected sampling data from this facility's system were used to develop the proposed LTM for cyanide.

The treatment performance data for Facility 30542 were evaluated and those data points which represent an effluent cyanide concentration in excess of 1.0 mg/L were removed from the dataset that represents best performance. Four of 36 effluent data points were removed based on this criterion. These batches should have been recycled to cyanide destruction treatment but were discharged at the time of the data collection due to a false negative result from the facility's internal test procedure (S102.1) for cyanide which did not identify the effluent concentrations above the 1.0 mg/L target.

The table below presents the cyanide destruction data identified as representing hydrogen peroxide oxidation with batch analysis using U.S. EPA Method 335.2 to ensure treatment concentrations below 1.0 mg/L prior to discharge.

Facility	Pollutant	Influent Conc. (mg/L)			Effluent Conc. (mg/L)			# of Data Points	Source
		Min.	Max.	Avg.	Min.	Max.	Avg.		
30542	Cyanide	160.0	3,700.0	1,937.4	0.005	0.720	0.25	32	SMD/I

SMD/I - Combined datasets from the Self-Monitoring Database and the EPA (List of Analytes) Sampling Program at Facility 30542, References 2, 3.

8.3.5 Steam Stripping and Distillation

The Agency collected steam stripping performance data from four EPA sampling episodes and from one EPA-sponsored pilot study.(5)(6)(7)(8)(9) The Agency also collected distillation performance data from one EPA-sponsored study.(10) The data from these sampling episodes and treatability studies were evaluated against the following criteria:

- Only those constituents proposed for regulation were included.
- Influent and effluent datasets from columns without trays or packing were excluded from consideration (i.e., no flash tanks).
- Influent and effluent datasets where the influent organic concentration was not detected were excluded from further consideration.
- Data were excluded if collected while a stripper was not at steady state. Steady state for the purpose of this comparison was defined as the point where temperatures and flow rates are constant.

The treatment performance data were then evaluated under two options:

1) Steam stripping option - under the steam stripping option all of the steam stripping performance data meeting the initial editing criteria were considered. Distillation performance data and treatment performance data showing no pollutant reduction were excluded. In addition, treatment performance data from columns with low steam rates were excluded as they are not representative of well designed, well operated systems. Steam

rate requirements are pollutant specific; steam rates were considered low if they were below the rates listed for each pollutant group in Table 10-8.

2) Steam stripping with distillation - under the steam stripping with distillation option the Agency only considered those data for each pollutant representing optimum performance of steam stripping and distillation technology. The methanol data collected as part of the alcohol distillation pilot study represents optimum performance for the removals of alcohols and other compounds with similar strippability. In addition, treatment performance data for other pollutants from columns with less than optimum steam rates were excluded because they are not representative of the performance basis of this option. Steam rate requirements are pollutant specific; steam rates were not considered optimum if they were less then rates presented for each pollutant group in Table 10-9.

Table 8-4 presents the steam stripping option data meeting the criteria listed above. Table 8-5 presents the steam stripping with distillation option data meeting the criteria listed above. For organic constituents, treatment performance data from facilities with operations in all subcategories were considered together since the treatment performance data do not indicate a difference in treatment based on subcategory. These data are considered representative of treatment performance for all subcategories.

The Agency has also evaluated the use of air stripping for the removal of ammonia.(9) Since the average ammonia concentration of the plant wastewater stream for the air stripping study was significantly less than that expected, the Agency made three test runs at varying V/L ratios with plant wastewater spiked with ammonia. The optimum V/L ratio for ammonia stripping in these runs was found to be 510 cfm/gpm and the treatment performance data from this run represent well-designed/well-operated treatment performance for ammonia removal. The treatment performance data from this run are presented below. The Agency is transferring this air stripping treatment performance data to represent treatment achievable by steam stripping and steam stripping with distillation. Each of these technologies are based on the same mass transfer principals and steam stripping and distillation are more effective treatment technologies than air stripping since they are conducted at elevated temperatures at

which ammonia is more volatile. Therefore, steam stripping and distillation will be as or more effective than air stripping in removing ammonia from wastewater. The air stripping data presented below are therefore being used to represent treatment performance achievable by steam stripping and distillation.

Facility	Pollutant	Influent Conc. (mg/L)			Effluent Conc. (mg/L)			# of Data Points	Source
		Min.	Max.	Avg.	Min.	Max.	Avg.		
30329	Ammonia (aqueous)	123.0	128.0	125.0	8.1	11.2	9.9	7	PILOT

PILOT - EPA-sponsored pilot study of air stripping, Reference 9.

8.3.6 Carbon Adsorption

In 1984, EPA's Water Engineering Research Laboratory (WERL) conducted pilot-plant activated carbon adsorption studies to determine constituents contributing to high COD in pharmaceutical manufacturing industry effluents, and to evaluate the ability of activated carbon adsorption to reduce COD levels.(11) The 1984 studies evaluated powdered activated carbon (PAC) addition to an activated sludge system (PACT®) and GAC treatment of pharmaceutical manufacturing plant secondary effluent. A follow-up study of PACT® was conducted in 1987.(12)

Data collected from the PACT® studies included raw waste and effluent pH, temperature, TSS, Total Chemical Oxygen Demand (TCOD), and Total Biochemical Oxygen Demand (TBOD). The follow-up study of PACT® treatment evaluated TCOD removal from pharmaceutical manufacturing wastewater and the efficiency of PAC in removing specific organics. Since the Agency is proposing GAC as part of its treatment options, PACT® treatment performance is not discussed further. The GAC study evaluated, on a pilot scale, the ability of GAC to remove TCOD from pharmaceutical manufacturing plant effluent.

The table below presents the GAC data available to the Agency from the 1984 study on TCOD removal. The Agency has used these TCOD data to develop a removal estimate of COD through GAC.

Pollutant	Run #	Influent Conc. (mg/L)			Effluent Conc. (mg/L)			# of Data Points	% Removal	Source
		Min.	Max.	Avg.	Min.	Max.	Avg.			
TCOD	1	730	1120	879	144	459	275	17	69	PILOT
TCOD	2	397	1940	917	123	897	432	42	53	PILOT

PILOT - EPA-sponsored pilot study of GAC, Reference 11.

8.4 Evaluation of Treatment Performance Data Transfers

The Agency does not have treatment performance data for all constituents and pollutant parameters proposed for regulation. The Agency is proposing to transfer treatment performance data from constituents with data to constituents without data that are deemed to be treated similarly. The transferred data are being used to develop limitations and standards for pollutants for which EPA does not have data. This section discusses the treatment performance data transfers proposed by the Agency.

8.4.1 Advanced Biological Treatment Performance Data Transfers

As shown in Table 8-2, EPA has performance data from advanced biological treatment for 29 of the organic constituents selected for regulation. To develop a basis of transfer for the other 24 organic constituents selected for regulation, the Agency grouped the organic constituents by structural and biodegradability groups and, in general, identified data transfers within these groups.

The organic constituents selected for regulation were grouped by biodegradability, including "high", "medium high", "medium", and "low" biodegradability. These

biodegradability groups were developed using Kmax values and the ratio of BOD_5 to theoretical oxygen demand (BOD_5/ThOD). The Kmax biodegradation rate is based on Monod-type kinetics, which assumes that biodegradation of any one constituent is independent of the concentrations of other constituents as long as no constituents are inhibitory or toxic to the microorganisms. Inhibition or toxicity by one constituent may slow or halt the degradation of other constituents. As the Kmax value increases, biodegradability increases. Large values of the ratio BOD_5/ThOD (e.g., >50%) indicate that the compound is readily biodegradable. Low ratios (e.g., < 20%) indicate that the compound is either slowly biodegradable or only partially biodegradable.(13)

Constituents were placed in the "high" biodegradability group if the Kmax value was greater than 4.00 E-06 or the BOD_5/ThOD ratio was greater than 50%. Because neither a Kmax value nor a BOD_5/ThOD ratio were found for methyl formate, this constituent was placed in the "high" group due to its similar structure to ethyl acetate which is in the "high" group.

Constituents were placed in the "medium high" biodegradability group if there was a broad range of BOD_5/ThOD ratios such that the range included both the medium and high categories (e.g., a BOD_5/ThOD ratio between 20% and 70%).

Constituents were placed in the "medium" biodegradability group if the Kmax value was greater than 1.00 E-07 and less than 4.00 E-06, or BOD_5/ThOD ratios were between 20 and 50 percent. Because Kmax values and BOD_5/ThOD ratios were not found for diethylamine, methylamine, 2-methylpyridine, and triethylamine, these constituents were placed in the "medium" group, based on the following information:

- Literature suggests biodegradability of diethylamine, but reports it is inhibitory to bacterial and algal cell division (14);
- Literature also suggests biodegradability of methylamine, but reports it is 50% inhibitory to nitrification (15);

- 2-methylpyridine is very similar in structure to pyridine, which is in the "high" group; however, 2-methylpyridine was placed in the "medium" group because the extra methyl group of this constituent makes it less biodegradable (16); and

- A 200 mg/L solution of triethylamine is 100% biodegraded but triethylamine is also reported to be 50% inhibitory to nitrifying bacteria.(15)

Constituents were placed in the "low" biodegradability group if the Kmax value was less than 1.00 E-07 or BOD_5/ThOD ratios were less than 20%. Because Kmax values and BOD_5/ThOD ratios were not found for amyl alcohol, formamide, and N,N-dimethylacetamide, these constituents were placed in the "low" group, based on the following information:

- Very slow biodegradation has been shown for amyl alcohol. An activated sludge unit demonstrated only 3.7% removal of ThoD of this compound in 24 hours.(15)

- Very slow biodegradation has been shown for formamide. An activated sludge unit demonstrated only 11.8% removal of ThOD of this compound in 24 hours.(15)

- N,N-Dimethylacetamide was placed in the "low" group due to its structural similarity to formamide.(15)

Table 8-6 presents the structural and biodegradability groups for ammonia and the organic constituents selected for regulation.

8.4.1.1 Data Transfer Methodology

Once the biodegradability groups were assigned, appropriate data transfers were identified whereby treatment performance data were transferred from constituents with data to constituents for which the Agency did not have data. In general, transfers were made between structurally similar constituents, mostly from within the same structural

group. Transfers were made from less treatable to more treatable constituents, based on their biodegradability groupings and general guidelines regarding biological treatability (i.e., decreasing biodegradability with increased branching or shortening of carbon chains).(16) Table 8-5 presents the proposed biological treatment performance data transfers. For some of the constituents listed in Table 8-5, treatment performance data were not available, and transfers of long-term means were not identified using the general methodology outlined above. Treatment performance data transfers were developed for these constituents based on the following methodology: transfers were still based on structural similarity, although a few of the transfers were not between constituents from the same structural group. Where more than one constituent was a candidate from which to transfer a long-term mean performance level, the constituent with the higher long-term mean was chosen. All of these transfers were between constituents that are similar in terms of relative biodegradability. The specific rationale supporting each data transfer is discussed below.

8.4.1.2 Alcohol Structural Group

The proposed data transfers within the alcohol structural group are from ethanol to ethylene glycol, tert-butyl alcohol, n-propanol, and amyl alcohol. In addition to having similar structures, ethylene glycol was included in the high biodegradability group while ethanol was included in the medium biodegradability group, suggesting a transfer of data from a more treatable to a less treatable constituent. Both n-propanol and amyl alcohol have similar structures to ethanol and have longer carbon chains, suggesting easier biodegradability. The transfer from ethanol to tert-butyl alcohol is based on structural similarity.

8.4.1.3 Aldehyde Structural Group

The proposed data transfer within the aldehyde structural group is from formaldehyde to isobutyraldehyde. Isobutyraldehyde has a longer carbon chain attached to the carbonyl

group, which should enhance its biodegradability. The ratio of BOD_5 to ThOD is 65% for isobutyraldehyde compared to 60% for formaldehyde, indicating isobutyraldehyde is as biodegradable as formaldehyde, thereby supporting this transfer.

8.4.1.4 Amide Structural Group

Within the amide structural group, the proposed data transfers are from N,N-dimethylformamide to N,N-dimethylacetamide and formamide. For N,N-dimethylacetamide, the additional methyl group attached to the acetamide should make it more biodegradable than N,N-dimethylformamide. For formamide, N,N-dimethylformamide is the most structurally similar constituent to this amide for which data are available.

8.4.1.5 Amine Structural Group

One constituent in the amine structural group, triethylamine, has best performer biotreatment data. However, the long-term mean for triethylamine is based on just two data points, with the effluent concentrations at the detection limit. Because of the limited nature of this dataset, the treatment performance data for triethylamine was not transferred to other pollutants. The amide, N,N-dimethylformamide, is proposed as a source of data transfer for methylamine and dimethylamine, since their structures are very similar. Both amines are less branched than N,N-dimethylformamide and, therefore, predicted to be more biodegradable than N,N-dimethylformamide.

8.4.1.6 Aromatic Structural Group

Within the aromatic structural group, data transfers are proposed from chlorobenzene to aniline, p-dichlorobenzene to o-dichlorobenzene, and 2-methylpyridine to N,N-dimethylaniline.

In the first transfer, the amino functional group in aniline is more easily biodegraded than the chlorine group in chlorobenzene. Also, these compounds have similar structures, and aniline, which is in the high biodegradability group, is predicted to be more biodegradable than chlorobenzene which is in the medium biodegradability group. Thus, with regard to the first data transfer, since chlorobenzene is less biodegradable than aniline, this data transfer is justified. As to the second transfer, p-dichlorobenzene data is transferred to o-dichlorobenzene based on similar structures. The third data transfer is based on the fact that N,N-dimethylaniline is closest in structure to 2-methylpyridine, an aromatic constituent for which treatment performance data are available.

8.4.1.7 Ester Structural Group

Data transfers are proposed in the ester structural group from isopropyl acetate to n-butyl acetate and from ethyl acetate to n-amyl acetate and methyl formate. For all three transfers, the constituent transferred is less complex and/or has a longer carbon chain attached to the ester group, making the constituents transferred easier to biodegrade.

8.4.1.8 Ether Structural Group

In the ether structural group, data transfers are proposed from tetrahydrofuran to polyethylene glycol 600, diethyl ether and isopropyl ether. The transfer from tetrahydrofuran to diethyl ether is based on the structural similarity of these constituents and the more highly branched structure of tetrahydrofuran. Both constituents have the same Kmax value, also supporting the rationale that diethyl ether should be at least as biodegradable as tetrahydrofuran. Tetrahydrofuran was chosen as the transfer basis for the other ethers without available treatment performance data since these constituents have similar structures and the long-term mean for tetrahydrofuran is slightly higher than that for 1,4-dioxane (the other ether with available treatment performance data).

8.4.1.9 Alkane Structural Group

In the alkane structural group, data transfers are proposed from n-hexane to cyclohexane and from toluene to petroleum naphtha. Cyclohexane and n-hexane are in the same structural group and both are considered highly biodegradable. Toluene, an aromatic compound, is the most structurally similar compound with performance data to petroleum naphtha. Petroleum naphtha, while placed in the alkane structural group, is actually a petroleum distillate fraction containing a mixture of aromatic and nonaromatic compounds, with characteristics similar to both alkanes and aromatics.

8.4.1.10 Miscellaneous Structural Group

From the miscellaneous structural group, treatment performance data transfers are proposed from ethanol to methyl cellosolve, from ethyl acetate to furfural, and from chloromethane to dimethyl sulfoxide. In each case, data were transferred from the most structurally similar constituent or group of constituents for which performance data are available.

8.4.2 Steam Stripping and Distillation Treatment Performance Data Transfers

The Agency has treatment performance data from well-designed/well-operated steam stripping units for ten of the organic constituents selected for regulation. To develop a basis of performance data transfer for the other 43 regulated organic constituents, the Agency grouped the organic constituents into strippability groups based on their Henry's Law Constant. Data transfers were then made within each group from the least strippable compound to more strippable compounds. The same methodology was followed for the steam stripping with distillation option where the Agency has treatment performance data from well-designed/well-operated steam stripping and distillation units for eight of the organic constituents selected for regulation.

Henry's Law is used to relate the equilibrium of the vapor-phase concentration of a solute to its liquid-phase concentration. In its traditional formulation, shown in Equation 8-1, Henry's Law expresses vapor-liquid equilibrium when the total pressure is low (less than 2 atm) and when the solute concentration is also low (less than 1 mol%).(19)

$$Xi \times H = Yi \times P \qquad (8\text{-}1)$$

Where: Xi = solute liquid-phase mole fraction
H = Henry's Law Constant
Yi = solute vapor-phase mole fraction
P = pressure.

While the solute concentration in the wastewater from facilities in the pharmaceutical manufacturing industry may be more than 1 mol%, Henry's Law Constants still provide a good measure of relative strippability, and can be used to rank the constituents and place them in strippability groups.

In environmental applications, Henry's Law is often used to relate the equilibrium vapor-phase concentration of a contaminant to its concentration in water. For a given contaminant in water, the Henry's Law Constant is directly proportional to the contaminant's vapor pressure and inversely proportional to its solubility. A contaminant with a high vapor pressure and low solubility in water has a high Henry's Law Constant. Conversely, a contaminant that has a low vapor pressure and/or is very soluble in water has a low Henry's Law Constant. For all contaminants, the Henry's Law Constant is a function of temperature and pressure.

These fundamental relationships allow Henry's Law Constants to be used to judge how effective treatment technologies that rely on liquid-to-vapor mass transfer will be and to judge the relative effectiveness of these technologies on different constituents. For example, constituents with high Henry's Law Constants are easily removed from water by

steam stripping or distillation, while constituents with low Henry's Law Constants are not.

Tables 8-7 and 8-8 present, for each regulated organic constituent and ammonia, the Henry's Law Constant (presented in decreasing order), the structural group, and the transfer group for the steam stripping and steam stripping with distillation options, respectively. In many cases, differing Henry's Law Constants for the same constituent were reported in differing data sources. In cases where different values were reported, those values presented in the EPA literature sources (20) or values from EPA's Surface Impoundment Modeling System (SIMS) database (18) were generally chosen as the preferred values. If no values were listed in any of these sources, then values were chosen from other sources based on best engineering judgment. All reported values for Henry's Law Constant are at 25°C and 1 atm (760 mmHg).

No Henry's Law Constants were found for polyethylene glycol 600 (PEG 600) and petroleum naphtha. PEG 600 is a mixture of condensation polymers of ethylene glycol with an average molecular weight of 600. The Henry's Law Constant for ethylene glycol, the "building block" of this polymer, was transferred to PEG 600 due to structural similarity. Petroleum naphtha is not a specific compound but a cut of petroleum that distills within a certain temperature range. Based on best engineering judgment, petroleum naphtha was placed in the "low" strippability group. The Henry's Law Constant for petroleum naphtha was transferred from the constituent with the lowest Henry's Law Constant in the "low" strippability group.

EPA has determined based on the Henry's Law constants and physical properties that eight of the constituents listed in Tables 8-7 and 8-8 are not strippable. These constituents cannot be treated by steam stripping and distillation and, therefore, do not have treatment performance data associated with stripping treatment. These constituents may be regulated under regulatory options which include biotreatment or granular

activated carbon but will not be regulated under regulatory options that include only steam stripping or steam stripping with distillation.

Sections 8.4.2.1 through 8.4.2.3 describe the steam stripping and steam stripping with distillation option treatment performance data transfers within each treatability group and the basic rationale behind each data transfer.

8.4.2.1 High Treatability Group (Steam Stripping and Steam Stripping with Distillation Options)

Three constituents with treatment performance data are included in the high treatability group, containing constituents which are easiest to strip. These constituents are chloroform, methylene chloride, and toluene. The long-term mean treatment performance level for methylene chloride, the least strippable of the constituents in the high treatability group, was transferred to the other, more strippable constituents in the high treatability group without treatment performance data. The long-term mean treatment performance level for methylene chloride is 0.10 mg/L for the steam stripping and steam stripping with distillation options.

8.4.2.2 Medium Treatability Group (Steam Stripping and Steam Stripping with Distillation Options)

Three constituents with treatment performance data, acetone, 2-butanone (also referred to as methyl ethyl ketone), and tetrahydrofuran are included in the medium treatability group. The long-term mean treatment performance level for acetone, the least strippable of the constituents in the medium treatability group, was transferred to the other, more strippable constituents in the medium treatability group without treatment performance data. The long-term mean treatment performance level for acetone is 3.0 mg/L under the steam stripping option, and 0.39 mg/L under the steam stripping with distillation option.

8.4.2.3 Low Treatability Group (Steam Stripping Option)

Treatment performance data are available for four constituents in the low treatability group: isopropanol, ethanol, pyridine, and methanol. The treatment performance data for isopropanol was transferred to more strippable constituents in the low treatability group for which treatment performance data is not available. The long-term mean treatment performance level for isopropanol is 76.3 mg/L. The treatment performance data for ethanol was transferred to n-propanol. The long-term mean treatment performance data for ethanol is 351 mg/L. Treatment performance data for methanol was transferred to the remaining constituents in the low treatability group for which no data were available. The long-term mean treatment performance level for methanol is 1,370 mg/L.

8.4.2.4 Low Treatability Group (Steam Stripping with Distillation Option)

Treatment performance data are available for two constituents in the low treatability group: pyridine and methanol. The treatment performance data for methanol, the least strippable of the constituents in the low treatability group, was transferred to the other, more strippable constituents in the low treatability group for which no treatment performance data were available. The long-term mean treatment performance level for methanol is 1.42 mg/L.

8.4.3 ASPEN Simulation Modelling to Support Steam Stripping with Distillation Treatment Performance Data Transfers

This section provides technical support for the data transfers made in developing the long-term mean treatment performance levels for the steam stripping with distillation treatment option. In particular, this section focuses on how process modeling was used to support the data transfers. Section 8.4.3.1 provides a general overview of the ASPEN simulation model. Section 8.4.3.2 describes the methodology used for supporting data

transfers for steam stripping with distillation. The results of the ASPEN simulations are presented in Section 8.4.3.3.

8.4.3.1 Overview of ASPEN

Since the 1970s, the process industries (chemical, petroleum, pharmaceutical, etc.) have increasingly relied on computer models to design and predict the performance of process equipment. The types of models typically used in these industries for this task are not statistical or empirical, but rely on engineering fundamentals such as the principles of thermodynamics and unit operations.

Two process models (also called process simulators) were used to support the development of the pharmaceutical manufacturing effluent guidelines: ASPEN/SP™ (Version 7.0) and ASPEN Plus™ (Version 8.5), commercial process design programs available respectively from Simulation Sciences, Inc. and Aspen Technologies, Inc. Both programs are descendants of the original ASPEN program which was developed at MIT during the period of 1976-1981 under the sponsorship of the Department of Energy and 55 industrial participants. Both programs give similar results and are widely accepted in industry for modeling chemical, petroleum, and environmental processes.

Key features of process simulation packages like ASPEN/SP™ and ASPEN Plus™ include the following:

- A large database of compounds and their properties which allow for modeling a wide range of processes;
- An extensive library of thermodynamic models (equations of state and activity coefficient models) for calculating the properties of mixtures; and
- A wide range of computer algorithms for modeling unit operations such as mixers, reactors, absorbers, strippers, and distillation columns.

8.4.3.2 Methodology for Data Transfer Simulations

As discussed previously, effluent data were collected on actual operating columns and pilot columns treating pharmaceutical manufacturing wastewater. For those pollutants where treatment performance data were not available, data were transferred from pollutants for which data were collected. The approach to making data transfers was two-part:

1) Transfers were made based on the physical properties that determine strippability, and

2) The proposed transfers were checked by simulating typical stripping systems using the ASPEN process simulators.

In using the ASPEN programs to support the data transfers, a five-step methodology was followed:

1) Each of the pollutants to be regulated was placed in one of seven strippability categories, with Group 1 representing pollutants that are most strippable and Group 7 representing pollutants that are not strippable.

2) Simple flowsheets for typical stripper systems were developed and the appropriate unit-operations models were selected.

3) Values were assumed for the key process variables (number of equilibrium stages and liquid to vapor (L/V) ratio). These key inputs vary among strippability groups because less strippable pollutants will operate at lower L/V ratios and require more stages. Influent concentrations for each pollutant were based on the maximum and average loadings reported in the Detailed Questionnaire.

4) The thermodynamic models for liquid-vapor equilibrium calculations were selected. To model the nonideal nature of most pollutants in water, an activity coefficient model was used.

5) The results of steps 1 through 4 were developed into simulation input files. Simulations were then run to determine if the transferred long-term mean performance level could be met by each pollutant assuming it was present at its maximum and average loading. If the long-term mean performance level could be met with either the maximum or average influent loading, the data transfer was considered acceptable. Note that in all cases the long-term mean performance level could be met at the maximum influent loads by increasing the number of stages or decreasing the L/V ratio assumed under step 3.

8.4.3.3 Strippability Groups

As discussed above, each of the pollutants proposed for regulation was placed in one of seven strippability groups. Placement was based on published Henry's Law Constants at 25°C and 1 atm. Table 8-9 presents these categories and the pollutants in each group. Note that these groups are different than the data transfer groups presented in Table 8-6, as they have been established for a different purpose. The data transfer groups presented in Table 8-8 were established for the purpose of transferring direct measurement data. The strippability groups discussed here were established for the purpose of assigning key process design variables for simulation purposes, and for cost estimating purposes, as discussed in Section 10.3.7. However, the grouping presented in Table 8-8 and these presented here share two important characteristics: (1) both grouping systems are based on a ranking of pollutants by Henry's Law constant from highest to lowest, and (2) pollutants considered not strippable are the same under both grouping systems.

8.4.3.4 Flowsheet Development

Two examples of typical distillation systems were identified: a stripper/decanter system for treating contaminants that have low water solubility and will form a phase-separable overhead product, and a distillation column with reflux for treating contaminants that are

highly water soluble and will not likely form a phase-separable overhead product. Figures 8-1 and 8-2 illustrate these process configurations.

Process simulation flowsheets were developed for these configurations. For modeling contaminants that form a phase-separable overhead product, the flowsheet in Figure 8-3 was used. In this flowsheet, the stripper was modeled using the equilibrium-stage distillation algorithm in ASPEN, RADFRAC. The decanter was modeled using the three-phase flash algorithm, FLASH3, and the feed/effluent exchanger was modeled with the heater algorithm, HEATER.

For modeling situations where the contaminants are highly water soluble, the flowsheet shown in Figure 8-4 was used. A reflux ratio high enough to achieve a concentrated overhead product (contaminant weight percent $\geq$ 33) was assumed.

The key part of the ASPEN simulations is the column calculations. The RADFRAC model, which makes these calculations, is a general distillation model which uses the equilibrium-stage concept.(30) The required inputs to model a distillation column using the RADFRAC model are the feed wastewater flow rate, the steam flow rate, the pressure drop across the column, and the number of equilibrium stages. The algorithm used in RADFRAC makes simultaneous mass and energy balances at each stage. This algorithm is based on the "inside-out" concept developed by Boston.(30) The distillation, absorption, and stripping models used in most process simulators utilize this approach.

8.4.3.5 Estimation of Key Input Variables

As previously noted, the two most important process variables which determine the removal efficiency of a steam stripper or a distillation column are: 1) the number of equilibrium stages, and 2) the L/V ratio in the column. Table 8-10 presents the number of equilibrium stages and L/V ratios assumed for each strippability group. The assumed

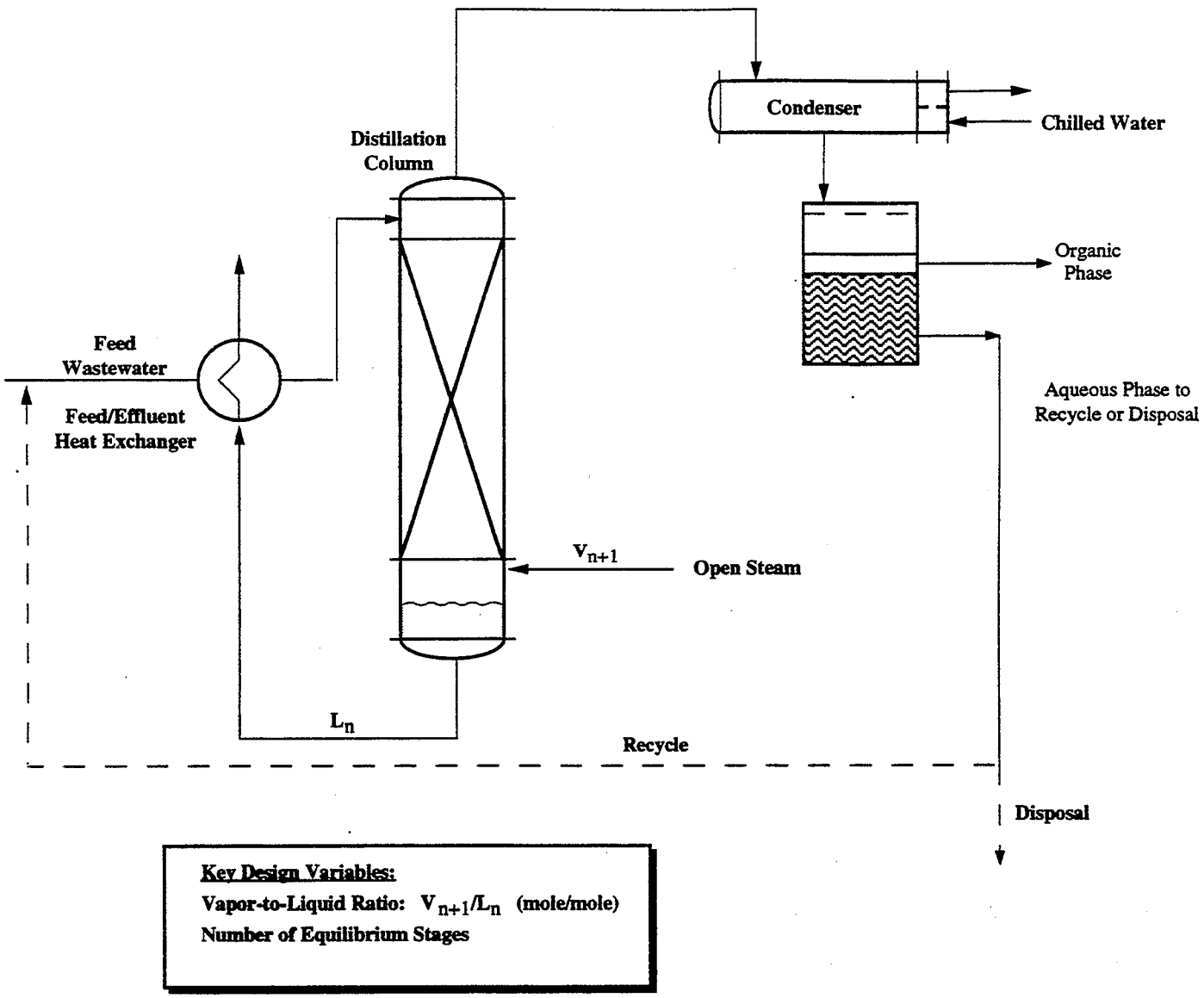
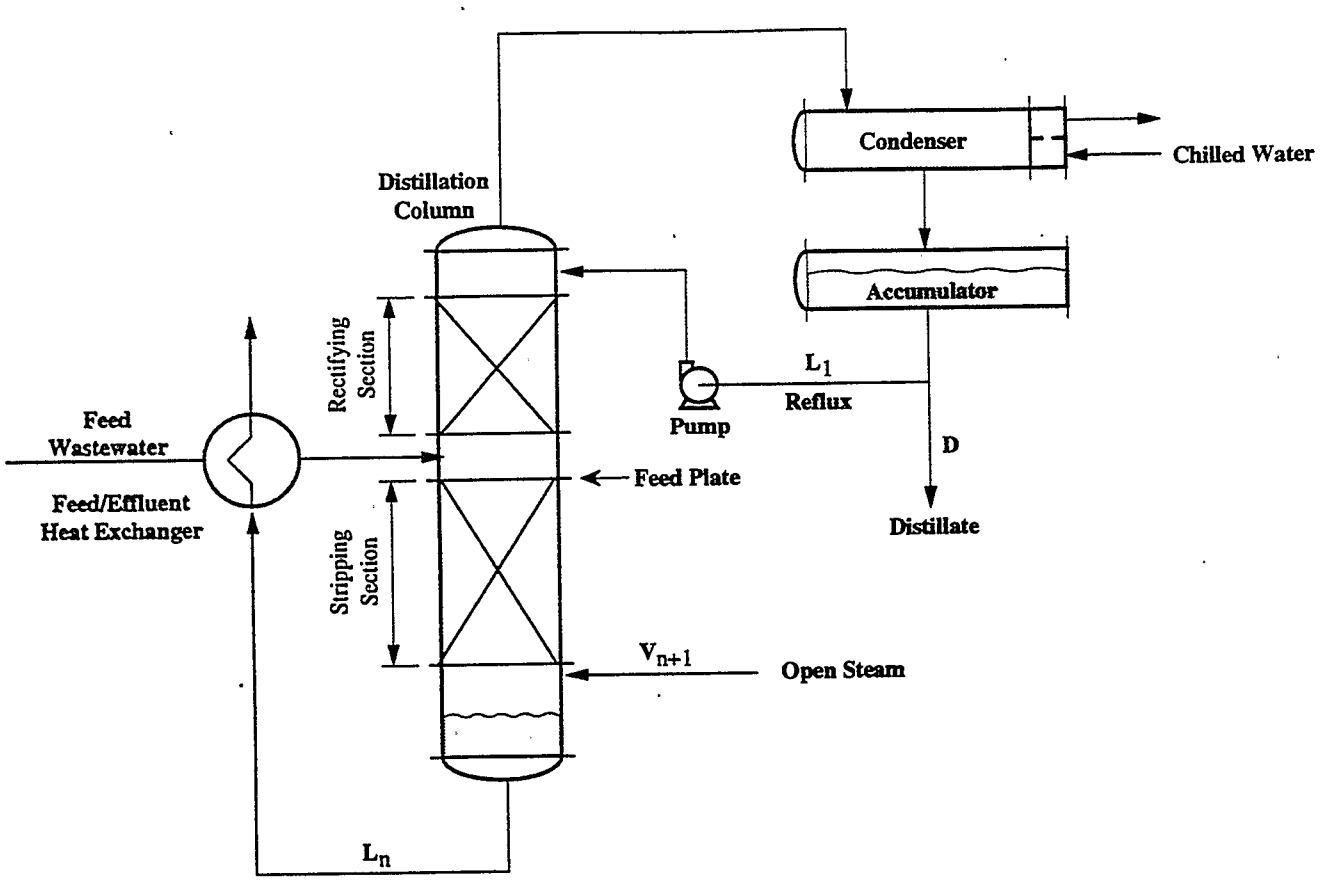


Figure 8-1. Process Schematic for a Steam Stripper with Open Steam



Key Design Variables:

Vapor-to-Liquid Ratio: V_{n+1}/L_n (mole/mole)

Reflux Ratio: L_1/D (mole/mole)

Number of Equilibrium Stages

Figure 8-2. Process Schematic for a Distillation Column with Open Steam

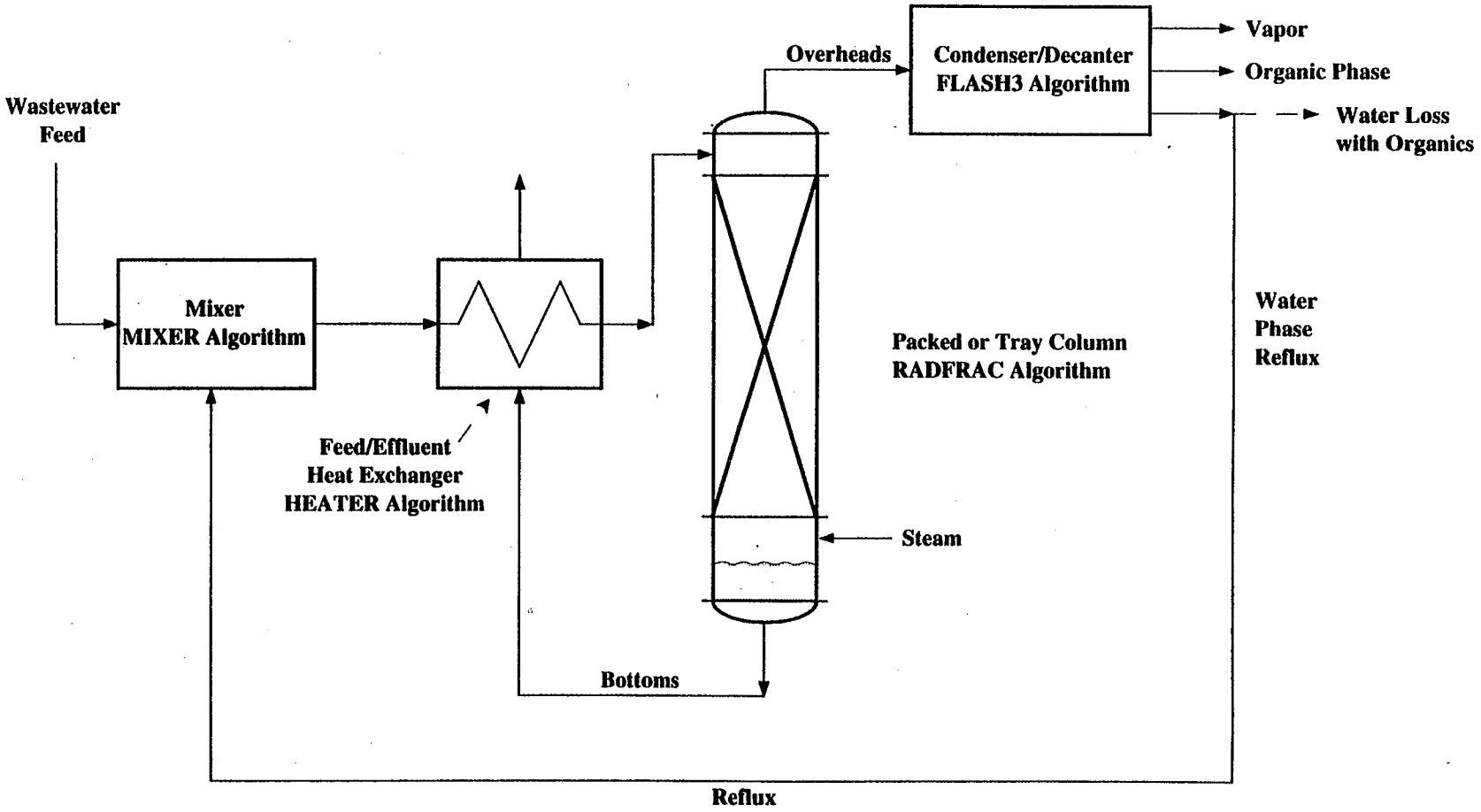


Figure 8-3. Simulation Block Diagram for Steam Stripper with Decanter

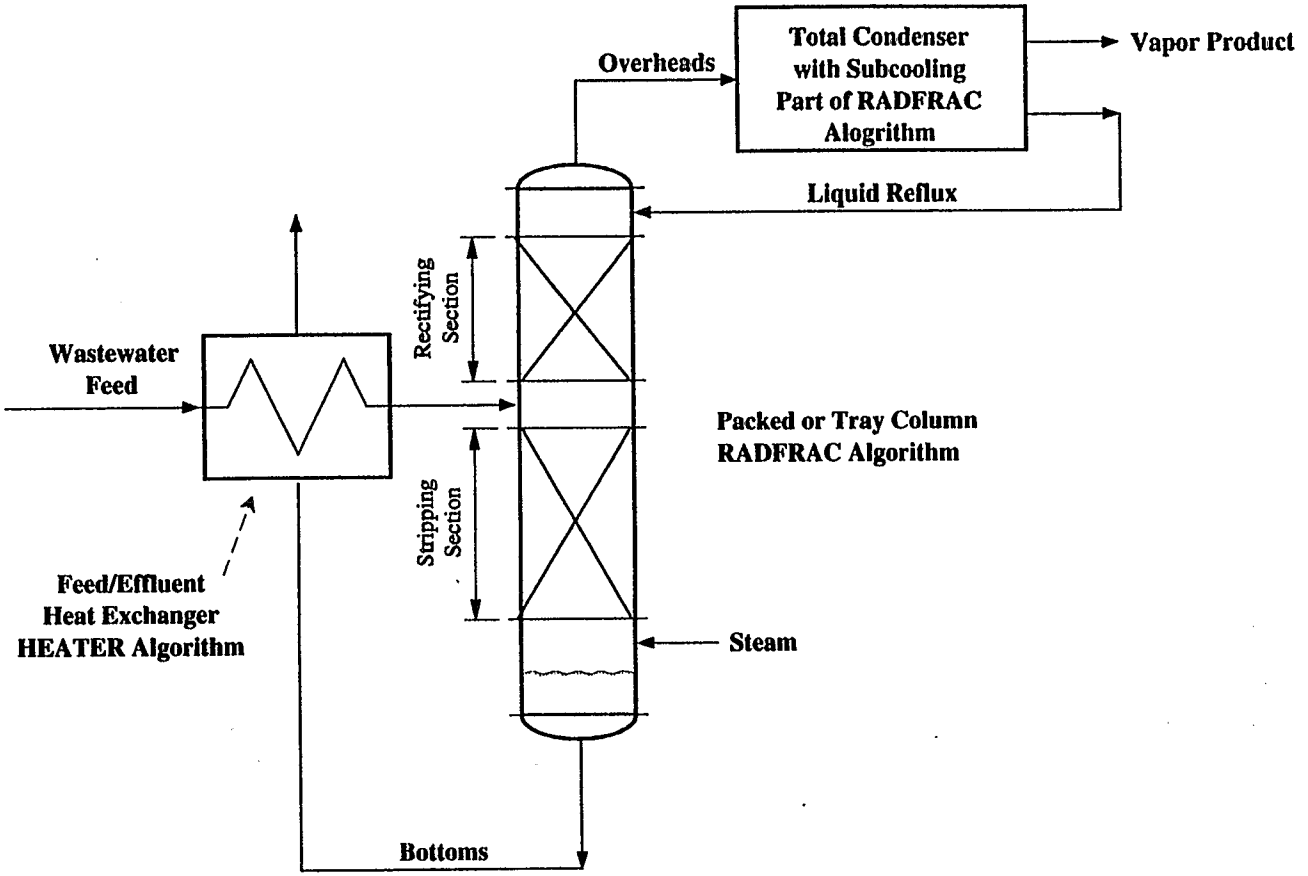


Figure 8-4. Simulation Block Diagram for Distillation Column with Open Steam

stages were chosen so that the total column height would be reasonable for a packed column assuming a height equivalent to one theoretical plate (HETP) of 2 to 3 feet. Two rectifying stages were assumed for strippability groups 3 through 6. The L/V ratios were then chosen to ensure high pollutant removal efficiencies. Other process inputs (feed water temperature, column pressure, condenser temperature, etc.) were based on typical industry values and are shown in Table 8-11. The values selected for these inputs will have less impact on the simulation results than the assumed number of stages or L/V ratio.

8.4.3.6 Selection of Thermodynamic Models

Since pharmaceutical manufacturing waste streams are generally nonideal mixtures, the liquid-vapor equilibrium calculations in the steam stripper simulations were performed using the UNIversal QUAsi Chemical (UNIQUAC) activity coefficient model. The UNIQUAC model is one of many commonly used activity coefficient models. It is a widely accepted tool for modeling nonideal solutions.

The UNIQUAC model uses binary interaction parameters in its calculations. These parameters can be determined from experimental vapor-liquid equilibrium data or they can be estimated using the UNIFAC group contribution method. With the UNIFAC method, the binary interaction between two compounds is estimated from the interactions between the different functional groups that make up the two compounds. The UNIFAC database, which consists of values for the interaction parameters between different functional groups, is available in several references.(24,27) For the ASPEN/SP™ simulations performed, the binary interaction parameters for the UNIQUAC model were taken either from the DECHEMA data series (26) or generated using UNIFAC. The validity of using UNIFAC was confirmed by comparing calculated K-values (estimated with ASPEN/SP™ using UNIFAC) to published K-values for several contaminants. Table 8-12 summarizes these results.

8.4.3.7 Summary of Simulation Results

Tables 8-13 and 8-14 present the results of the treatment performance data transfer simulation runs for Subcategory A and/or C facilities and Subcategory B and/or D facilities, respectively. These results show that simulating the average pollutant loading will result in an effluent concentration from steam stripping with distillation less than the pollutant's proposed long-term mean performance level for steam stripping with distillation. The Agency also found that in almost all cases simulating the maximum pollutant loading would also result in effluent concentrations less than the proposed long-term mean performance levels. Since transfers of experimental data were made from pollutants that are less strippable (i.e., a lower Henry's Law Constant) to pollutants that are more strippable, the effluent limitations guidelines should be attainable for all pollutants where well-designed, well-operated steam stripping and distillation columns are installed.

8.5 Long-Term Mean Development for Conventional Pollutant Parameters and COD

The conventional pollutants BOD_5 and TSS along with the nonconventional pollutant COD would be controlled as follows under the regulatory options considered for the pharmaceutical manufacturing industry.

Subcategory	Discharge Status	Regulatory Option	Pollutant Parameters Controlled
A and C	Direct	BPT Option 1	BOD_5, COD, TSS
A and C	Direct	BPT Option 2	BOD_5, COD, TSS
A and C	Direct	BPT Option 3	BOD_5, COD, TSS
A and C	Direct	BPT Option 4	BOD_5, COD, TSS
A and C	Direct	BPT Option 5	BOD_5, COD, TSS
A and C	Direct	BCT Option 1	BOD_5, TSS
A and C	Direct	BCT Option 2	BOD_5, TSS
A and C	Direct	BCT Option 3	BOD_5, TSS

Subcategory	Discharge Status	Regulatory Option	Pollutant Parameters Controlled
A and C	Direct	BCT Option 4	BOD_5, TSS
A and C	Direct	BCT Option 5	BOD_5, TSS
A and C	Direct	BAT Option 1	COD
A and C	Direct	BAT Option 2	COD
A and C	Direct	BAT Option 3	COD
A and C	Direct	BAT Option 4	COD
A and C	Direct	NSPS Option 1	BOD_5, COD, TSS
A and C	Direct	NSPS Option 2	BOD_5, COD, TSS
B and D	Direct	BPT Option 1	BOD_5, COD, TSS
B and D	Direct	BPT Option 2	BOD_5, COD, TSS
B and D	Direct	BPT Option 3	BOD_5, COD, TSS
B and D	Direct	BCT Option 1	BOD_5, TSS
B and D	Direct	BCT Option 2	BOD_5, TSS
B and D	Direct	BCT Option 3	BOD_5, TSS
B and D	Direct	BAT Option 1	COD
B and D	Direct	BAT Option 2	COD
B and D	Direct	BAT Option 3	COD
B and D	Direct	BAT Option 4	COD
B and D	Direct	NSPS Option 1	BOD_5, COD, TSS
B and D	Direct	NSPS Option 2	BOD_5, COD, TSS

Using the treatment performance data presented in Sections 8.3.1, 8.3.2, and 8.3.3, a statistical analysis of the data was conducted to develop a long-term mean concentration and variability factors for BOD_5, TSS, and COD under each of the regulatory options listed above, except BPT Option 1 and BCT Option 1. BPT Option 1 and BCT Option 1 is equivalent to current performance and no statistical analysis of this level were performed. A detailed description of the statistical analysis and the results from this analysis are presented in Statistical Support Document for the Proposed Effluent Limitations Guidelines for the Pharmaceutical Manufacturing Industry (31) (hereafter referred to as the Statistical Support Document).

To develop the concentration-based long-term means and variability factors for each pollutant parameter, EPA modeled the concentration data using a modification of the delta-lognormal distribution. The modified delta-lognormal distribution model assumes that all nondetects occur at the detection limit and that the measured concentrations follow a lognormal distribution (i.e., the logarithms of the measured data are normally distributed). The modified delta-lognormal distribution is identical to a lognormal distribution if there are no nondetects in the data.

Table 8-15 presents the long-term mean treatment performance concentrations for BOD_5, COD, and TSS based on the datasets identified in Section 8.2.

8.6 Long-Term Mean Development for Cyanide

Cyanide is controlled in the following regulatory options for the pharmaceutical manufacturing industry.

Subcategory	Discharge Status	Regulatory Option
A and C	Direct	BPT Option 2
A and C	Direct	BPT Option 3
A and C	Direct	BPT Option 4
A and C	Direct	BPT Option 5
A and C	Direct	BAT Option 1
A and C	Direct	BAT Option 2
A and C	Direct	BAT Option 3
A and C	Direct	BAT Option 4
A and C	Direct	NSPS Option 1
A and C	Direct	NSPS Option 2
A and C	Indirect	PSES Option 1
A and C	Indirect	PSES Option 2
A and C	Indirect	PSES Option 3
A and C	Indirect	PSNS Option 1
A and C	Indirect	PSNS Option 2
A and C	Indirect	PSNS Option 3

Using the treatment performance data presented in Section 8.3.4, a statistical analysis of the data was conducted to develop a long-term mean concentration and variability factors for cyanide. The long-term mean concentration developed for cyanide is 0.24 mg/L. A detailed description of the statistical analysis and the results from this analysis are presented in the Statistical Support Document. The proposed regulation does not propose cyanide limitations or standards for subcategories B and D because cyanide is not present in the wastewaters of those facilities.

8.7 Development of Long-Term Mean Concentrations for Priority and Nonconventional Pollutants

Sections 6.6 and 6.7 list the priority and nonconventional pollutants selected for regulation in the pharmaceutical manufacturing industry. Priority and nonconventional pollutants are controlled in the following regulatory options.

Subcategory	Discharge Status	Regulatory Option	Technology(ies) Controlling the Pollutant Parameters
A and C	Direct	BAT Option 1	Adv. BT
A and C	Direct	BAT Option 2	Steam Stripping + Adv. BT
A and C	Direct	BAT Option 3	SS/Distillation + Adv. BT
A and C	Direct	BAT Option 4	SS/Distillation + Adv. BT + GAC
A and C	Direct	NSPS Option 1	SS/Distillation + Adv. BT
A and C	Direct	NSPS Option 2	SS/Distillation + Adv. BT + GAC
A and C	Indirect	PSES Option 1	Steam Stripping
A and C	Indirect	PSES Option 2	SS/Distillation
A and C	Indirect	PSES Option 3	SS/Distillation + Adv. BT
A and C	Indirect	PSES Option 4	SS/Distillation + Adv. BT + GAC
A and C	Indirect	PSNS Option 1	SS/Distillation
A and C	Indirect	PSNS Option 2	SS/Distillation + Adv. BT
A and C	Indirect	PSNS Option 3	SS/Distillation + Adv. BT + GAC
B and D	Direct	BAT Option 1	Adv. BT
B and D	Direct	BAT Option 2	Steam Stripping + Adv. BT
B and D	Direct	BAT Option 3	SS/Distillation + Adv. BT

Subcategory	Discharge Status	Regulatory Option	Technology(ies) Controlling the Pollutant Parameters
B and D	Direct	BAT Option 4	SS/Distillation + Adv. BT + GAC
B and D	Direct	NSPS Option 1	SS/Distillation + Adv. BT
B and D	Direct	NSPS Option 2	SS/Distillation + Adv. BT + GAC
B and D	Indirect	PSES Option 1	Steam Stripping
B and D	Indirect	PSES Option 2	SS/Distillation
B and D	Indirect	PSES Option 3	SS/Distillation + GAC
B and D	Indirect	PSNS Option 1	SS/Distillation
B and D	Indirect	PSNS Option 2	SS/Distillation + GAC

Adv. BT - Advanced Biological Treatment.
Steam Stripping = In-plant Steam Stripping
SS/Distillation - In-plant Steam Stripping with Distillation.
GAC - Granular Activated Carbon.

The statistical development of long-term mean concentrations for these priority and nonconventional pollutants (excluding cyanide and ammonia) is presented in Section 8.7.1. Section 8.7.2 discusses the methodology used by the Agency to develop long-term mean concentrations for these pollutants under the treatment trains of in-plant steam stripping followed by advanced biological treatment and in-plant steam stripping with distillation followed by advanced biological treatment. Section 8.7.3 presents the development of a long-term mean concentration for ammonia.

8.7.1 Statistical Development of Long-Term Mean Concentrations for Priority and Nonconventional Pollutants

Using the treatment performance data presented in Sections 8.3.1 and 8.3.5, the Agency conducted a statistical analysis of the data to develop a long-term mean and variability factors for those priority and nonconventional pollutants with advanced biological, steam stripping, and steam stripping with distillation treatment performance data. A detailed description of the statistical analysis and the results from this analysis are presented in the Statistical Support Document. Table 8-16 presents the long-term mean

concentrations developed for these pollutants using the datasets identified in Tables 8-2, 8-4, and 8-5.

For priority and nonconventional pollutants without advanced biological, steam stripping, or distillation treatment performance data, a transfer was applied as discussed in Section 8.4. Table 8-17 presents the long-term mean treatment performance concentrations for priority and nonconventional pollutants after application of the treatment performance data transfers.

8.7.2 Methodology Used to Develop Long-term Mean Treatment Performance Concentrations for In-plant Steam Stripping and In-plant Steam Stripping with Distillation Followed by Advanced Biological Treatment

The Agency does not have end-of-pipe treatment performance data for priority and nonconventional pollutants representative of the combined treatment train of in-plant steam stripping at all necessary locations followed by advanced biological treatment or in-plant steam stripping with distillation at all necessary locations followed by advanced biological treatment. Therefore, the performance of these combined treatment trains were calculated from available treatment performance data for steam stripping, steam stripping with distillation, and advanced biological treatment technology. The following methodology was used to develop long-term mean treatment performance concentrations for priority and nonconventional pollutants under these treatment trains:

1. The long-term mean treatment performance concentrations for steam stripping and steam stripping with distillation shown on Table 8-17 were used to represent the concentration of priority and nonconventional pollutants after application of in-plant steam stripping and steam stripping with distillation technology;

2. Percent removals associated with each dataset listed in Table 8-2 were calculated for those pollutants with advanced biological treatment performance data;

3. For each pollutant, the highest advanced biological treatment percent removal from the available datasets was determined;

4. For those pollutants without treatment performance data, percent removals were transferred from those pollutants with data following the treatment data transfer methodology discussed in Section 8.4.1;

5. The percent removal achievable through advanced biological treatment established in steps 3 and 4 were applied to the in-plant steam stripping and steam stripping with distillation long-term mean concentrations; and

6. The resulting long-term mean concentrations represent the long-term mean concentrations achievable after the application of steam stripping and steam stripping with distillation followed by advanced biological treatment.

Tables 8-18 and 8-19 present the results of these calculations.

8.8 Long-Term Mean Development for Ammonia

Ammonia is controlled in the following regulatory options for the pharmaceutical manufacturing industry.

Subcategory	Discharge Status	Regulatory Option
A and C	Direct	BAT Option 1
A and C	Direct	BAT Option 2
A and C	Direct	BAT Option 3
A and C	Direct	BAT Option 4
A and C	Direct	NSPS Option 1
A and C	Direct	NSPS Option 2
A and C	Indirect	PSES Option 1
A and C	Indirect	PSES Option 2
A and C	Indirect	PSES Option 3
A and C	Indirect	PSES Option 4
A and C	Indirect	PSNS Option 1
A and C	Indirect	PSNS Option 2
A and C	Indirect	PSNS Option 3

Advanced biological treatment performance data for ammonia are presented in Section 8.3.1. Air stripping treatment performance data for ammonia are presented in Section 8.3.5; the air stripping data are being used to represent treatment achievable by steam stripping and distillation. A detailed description of the statistical analysis of these data and the results from this analysis are presented in the Statistical Support Document. EPA does not propose to control ammonia for Subcategories B and D because ammonia is not present in Subcategory B and D wastewaters at concentrations of concern.

The long-term mean treatment performance concentration developed for ammonia through advanced biological treatment is 2.56 mg/L. The long-term mean treatment performance concentration for ammonia applicable to steam stripping and steam stripping with distillation treatment is 9.91 mg/L.

Table 8-1

Advanced Biological Treatment Performance Data for BOD_5, COD, and TSS

Facility	Pollutant	Influent Conc. (mg/L)			Effluent Conc. (mg/L)			# of Effluent Data Points	Source
		Min.	Max.	Avg.	Min.	Max.	Avg.		
50002	BOD_5	10	2,080	971	3.0	174	40.3	354	SMD
	COD	157	3,750	2,030	58.0	1,010	374	359	SMD
	TSS	-	-	-	8.0	604	101	107	SMD
50003	BOD_5	230	9,730	2,440	16.0	809	74.3	365	SMD
	COD	526	12,000	4,960	197	10,100	744	365	SMD
	TSS	-	-	-	16.3	2,710	155	365	SMD
50004	BOD_5	700	14,100	5,750	0.8	19.7	4.7	356	SMD
	COD	1,450	14,000	9,190	27.9	189	98.3	51	SMD
	TSS	-	-	-	0.5	254	18.7	356	SMD
50005	BOD_5	566	5,880	2,620	16.0	660	77.8	366	SMD
	COD	986	11,600	5,280	108.0	1,700	883	366	SMD
	TSS	-	-	-	8.0	577	106	366	SMD
50007	BOD_5	140	2,940	1,220	3.0	81.6	20.1	228	SMD
	COD	436	28,200	3,420	108	1,160	416	605	SMD
	TSS	24.0	40,400	655	4.0	158	30.4	951	SMD
50008	BOD_5	49.2	857	323	0.9	29.8	6.7	51	SMD
	COD	126	1,580	762	3.0	70.0	17.1	63	SMD
	TSS	48.0	672	214	1.0	41.5	7.7	51	SMD
50011	BOD_5	92.0	1,100	259	1.0	26.0	7.7	42	SMD
	COD	240	1,100	548	20.0	260	74.6	38	SMD
	TSS	-	-	-	5.0	120	28.4	42	SMD

Source:
SMD - Self-Monitoring Database, Reference 2.

Table 8-2

Advanced Biological Treatment Performance Data for Priority and Nonconventional Pollutants

Facility	Pollutant	Influent Conc. (mg/L)			Effluent Conc. (mg/L)			# of Effluent Data Points	Source
		Min.	Max.	Avg.	Min.	Max.	Avg.		
30540	Acetone	38.5	112	61.8	0.05	0.800	0.137	10	I
30623	Acetone	1.30	14.9	6.78	0.05	0.130	0.066	19	I
30701	Acetone	1.0	442	65.0	1.0	8.0	1.08	242	P
30949	Acetone	4,810	4,810	4,810	0.029	0.150	0.090	2	3
30623	Acetonitrile	0.005	1.62	0.337	0.005	0.005	0.005	19	I
30540	Benzene	1.6	1.6	1.6	0.010	0.010	0.010	1	S
30540	Benzene	0.127	0.127	0.127	0.040	0.040	0.040	1	A
30600	Benzene	0.260	0.260	0.260	0.120	0.120	0.120	1	S
30623	Benzene	1.0	41.0	14.3	0.002	0.002	0.002	3	P
30623	Benzene	0.120	0.120	0.120	0.010	0.010	0.010	1	S
30701	Benzene	0.048	0.820	0.434	0.00001	0.00001	0.00001	2	S
30949	n-Butanol	103	103	103	0.25	0.25	0.25	2	3

Table 8-2

(Continued)

Facility	Pollutant	Influent Conc. (mg/L)			Effluent Conc. (mg/L)			# of Effluent Data Points	Source
		Min.	Max.	Avg.	Min.	Max.	Avg.		
30623	2-Butanone (MEK)	13.7	107	35.7	0.050	0.065	0.051	19	I
30623	Chlorobenzene	6.4	6.4	6.4	0.010	0.010	0.010	1	S
30050	Chloroform	3.17	3.17	3.17	0.0081	0.0081	0.0081	1	S
30050	Chloroform	0.554	1.62	1.09	0.001	0.001	0.001	3	V
30540	Chloroform	1.47	5.51	3.18	0.010	0.010	0.010	10	I
30540	Chloroform	0.370	0.370	0.370	0.010	0.010	0.010	1	S
30600	Chloroform	0.180	0.180	0.180	0.110	0.110	0.110	1	S
30623	Chloroform	1.00	16.0	6.3	0.009	0.018	0.013	3	P
30623	Chloroform	0.202	55.3	7.62	0.010	0.024	0.013	19	I
30701	Chloroform	0.007	1.05	0.529	0.90	2.80	1.85	2	S
31108	Chloroform	70.0	70.0	70.0	0.0017	0.220	0.111	2	3

Table 8-2

(Continued)

Facility	Pollutant	Influent Conc. (mg/L)			Effluent Conc. (mg/L)			# of Effluent Data Points	Source
		Min.	Max.	Avg.	Min.	Max.	Avg.		
0540	Chloromethane (Methyl chloride)	4.70	5.33	5.03	0.010	0.124	0.053	10	I
30623	Chloromethane (Methyl chloride)	0.117	0.978	0.550	0.050	0.050	0.050	19	I
31108	1,4-Dichlorobenzene	57.0	57.0	57.0	0.001	0.001	0.001	2	3
30623	1,2-Dichloroethane	0.132	24.8	13.0	0.010	0.263	0.064	19	I
30623	1,2-Dichloroethane	11.0	11.0	11.0	0.50	0.50	0.50	1	S
30623	1,2-Dichloroethane	1.00	5.00	2.67	0.002	0.110	0.038	3	P
30623	N,N-Dimethylformamide	0.10	113	49.8	0.010	0.035	0.011	20	I
30540	1,4-Dioxane	0.010	574	57.4	0.010	0.463	0.055	10	I

Table 8-2

(Continued)

Facility	Pollutant	Influent Conc. (mg/L)			Effluent Conc. (mg/L)			# of Effluent Data Points	Source
		Min.	Max.	Avg.	Min.	Max.	Avg.		
30540	Ethanol	124	209	161	0.500	5.51	1.00	10	I
30623	Ethanol	10.6	1,320	253	0.500	0.800	0.530	20	I
30701	Ethanol	1.00	791	130	1.00	10.0	1.07	242	P
30540	Ethyl acetate	40.0	77.1	57.9	0.500	0.600	0.510	10	I
30701	Ethyl acetate	1.00	260	15.5	1.00	1.00	1.00	242	P
30623	Formaldehyde	0.300	6.50	1.75	0.120	0.800	0.343	19	I
30623	Heptane	0.005	3.25	0.921	0.005	0.005	0.005	19	I
30623	Hexane	0.046	1.43	0.444	0.005	0.005	0.005	19	I
30540	Isopropanol	112	152	136	0.500	0.500	0.500	10	I
30949	Isopropanol	2,560	2,560	2,560	0.025	0.100	0.062	2	3
30540	Isopropyl acetate	26.4	112	68.1	0.500	0.500	0.500	10	I

Table 8-2

(Continued)

Facility	Pollutant	Influent Conc. (mg/L)			Effluent Conc. (mg/L)			# of Effluent Data Points	Source
		Min.	Max.	Avg.	Min.	Max.	Avg.		
30540	Methanol	165	1,100	592	2.26	87.6	13.6	10	I
30623	Methanol	8.50	16,000	1,900	0.300	3.70	0.650	20	I
30701	Methanol	1.00	49.0	13.9	1.00	1.00	1.00	242	P
30349	Methylene chloride	0.800	0.800	0.800	0.250	0.250	0.250	1	S
30540	Methylene chloride	14.0	14.0	14.0	0.140	0.140	0.140	1	S
30600	Methylene chloride	6.20	6.20	6.20	2.60	2.60	2.60	1	S
30623	Methylene chloride	1.00	264.0	91.0	0.004	0.110	0.069	3	P
30623	Methylene chloride	36.9	1,340	416	0.010	1.10	0.110	19	I
30623	Methylene chloride	0.170	0.170	0.170	0.010	0.010	0.010	1	S
30704	Methylene chloride	135	135	135	0.040	0.040	0.040	1	3
30949	Methylene chloride	3,380	3,380	3,380	0.017	0.022	0.020	2	3
30540	Methyl isobutyl ketone	0.050	1.21	0.322	0.050	0.050	0.050	10	I
30949	Methyl isobutyl ketone	1,430	1,430	1,430	0.010	0.010	0.010	2	3

Table 8-2

(Continued)

Facility	Pollutant	Influent Conc. (mg/L)			Effluent Conc. (mg/L)			# of Effluent Data Points	Source
		Min.	Max.	Avg.	Min.	Max.	Avg.		
30540	2-Methylpyridine	0.941	4.08	2.83	0.050	0.050	0.050	10	I
30050	Phenol	0.099	0.632	0.366	0.003	0.003	0.003	2	V
30623	Phenol	1.40	1.40	1.40	0.010	0.010	0.010	1	S
30623	Phenol	0.010	0.651	0.169	0.010	0.025	0.012	20	I
30949	Pyridine	1.53	1.53	1.53	0.010	0.010	0.010	2	3
30623	Tetrahydrofuran	1.59	75.0	25.4	0.005	3.48	1.22	20	I
30050	Toluene	0.470	0.470	0.470	0.00001	0.00001	0.00001	1	S
30050	Toluene	0.078	0.193	0.131	0.001	0.001	0.001	3	V
30540	Toluene	0.146	0.484	0.311	0.010	0.010	0.010	10	I
30600	Toluene	0.310	0.310	0.310	0.180	0.180	0.180	1	S
30623	Toluene	11.0	11.0	11.0	0.010	0.010	0.010	1	S
30623	Toluene	1.21	38.0	10.4	0.010	0.010	0.010	19	I

Table 8-2

(Continued)

Facility	Pollutant	Influent Conc. (mg/L)			Effluent Conc. (mg/L)			# of Effluent Data Points	Source
		Min.	Max.	Avg.	Min.	Max.	Avg.		
30623	Toluene	1.0	4.0	2.33	0.002	0.053	0.019	3	P
30701	Toluene	0.170	10.4	5.28	0.00001	0.00001	0.00001	2	S
30701	Toluene	1	294	4.57	1.00	1.00	1.00	242	P
30540	Trichlorofluoromethane	1.32	2.25	1.77	0.010	0.043	0.018	10	I
30600	Trichlorofluoromethane	0.970	0.970	0.970	0.420	0.420	0.420	1	S
30949	Triethylamine	818	818	818	0.050	0.050	0.050	2	3
30540	Xylenes	2.01	10.6	5.50	0.010	0.010	0.010	10	I

Sources:
A - ADA Study.
I - EPA (List of Analytes) Sampling Program.
P - Facility Self-Monitoring Data from 1989 Pretest Questionnaires.
S - Screening Sampling Program.
V - Verification Sampling Program.
3 - Facility Self-Monitoring Data/Estimated Average Influent Concentrations.

Note: Values that were not detected were set at the detection limit.

Table 8-3

Multimedia Filtration Treatment Performance Data for TSS

Facility	Pollutant	Influent Conc. (mg/L)			Effluent Conc. (mg/L)			# of Effluent Data Points	Source
		Min.	Max.	Avg.	Min.	Max.	Avg.		
50007	TSS	4.0	110	24.2	2.0	60.0	12.8	466	SMD
12053	TSS	5.5	106	26.2	0.40	35.0	6.84	84	SRI
12317	TSS	1.0	83.0	18.8	1.0	41.0	5.87	248	SRI

SMD - Self-Monitoring Database, Reference 2.
SRI - Self-Monitoring Database from the 10/27/83 NSPS proposed rule containing facility self-monitoring data from 1982 and 1983, Reference 4.

Note: Values that were not detected were set at the detection limit.

Table 8-4

Well-Designed/Well-Operated Steam Stripping Treatment Performance Data for Priority and Nonconventional Pollutants

Facility-Stream	Pollutant	Influent Conc. (mg/L)			Effluent Conc. (mg/L)			# of Effluent Data	Source
		Min.	Max.	Avg.	Min.	Max.	Avg.	Points	
60000-A	Acetone	731	1,570	1,020	0.197	9.68	3.00	16	I
30329-B	2-Butanone	2,670	35,300	17,500	4.70	392	121	11	I
60000-A	Chloroform	272	1,170	759	0.010	0.010	0.010	16	I
60000-B	Chloroform	80.5	85.0	82.7	0.010	0.010	0.010	8	I
30329-B	Ethanol	1,190	28,100	13,400	102	1,330	693	11	I
60000-A	Ethanol	280	660	418	0.500	36.0	8.23	16	I
30329-B	Isopropanol	427	10,900	5,200	22.4	370	146	11	I
60000-A	Isopropanol	950	2,200	1,520	0.500	21.9	6.12	16	I
60000-C	Methanol	5,300	7,000	6,660	120	3,900	1,370	5	I
60000-A	Methanol	1,450	3,700	2,430	46.0	1,300	474	16	I
60000-B	Methanol	100,000	240,000	182,000	60,000	120,000	85,000	8	I

Table 8-4

(Continued)

Facility-Stream	Pollutant	Influent Conc. (mg/L)			Effluent Conc. (mg/L)			# of Effluent Data Points	Source
		Min.	Max.	Avg.	Min.	Max.	Avg.		
60000-A	Methylene chloride	17.1	54.0	32.7	0.010	0.398	0.058	16	I
30487-A	Methylene chloride	8.62	55.8	21.0	0.100	0.101	0.100	23	I
30618-A	Methylene chloride	6,580	12,800	9,660	1.00	10.0	3.84	19	I
30487-A	Pyridine	7.75	7.75	7.75	1.0	1.0	1.0	1	I
60000-C	Tetrahydrofuran	7,500	8,550	8,340	0.22	2.57	1.54	5	I
30329-B	Toluene	252	252	252	0.124	2.41	1.13	6	I
60000-C	Toluene	515	580	528	0.333	0.630	0.473	5	I
60000-A	Toluene	16.7	21.3	18.6	0.010	0.042	0.022	16	I
60000-B	Toluene	237	668	494	0.010	0.012	0.010	8	I
30487-A	Toluene	15.2	82.6	35.2	0.100	0.100	0.100	23	I

Sources:
I - EPA (List of Analytes) Sampling Program, Reference 3.

Note: Values that were not detected were set at the detection limit.

Table 8-5

Well-Designed/Well-Operated Steam Stripping with Distillation Treatment Performance Data for Priority and Nonconventional Pollutants

Facility-Stream	Pollutant	Influent Conc. (mg/L)			Effluent Conc. (mg/L)			# of Effluent Data	Source
		Min.	Max.	Avg.	Min.	Max.	Avg.	Points	
60000-A	Acetone	731	769	746	0.197	0.769	0.389	8	I
30329-B	2-Butanone	2,670	35,300	26,000	4.7	99.4	25.8	7	I
60000-A	Chloroform	272	1,170	759	0.010	0.010	0.010	16	I
60000-B	Chloroform	80.5	85.0	82.7	0.010	0.010	0.010	8	I
60001-A	Methanol	10,300	42,100	22,500	0.50	11.1	1.52	65	R
60000-A	Methylene chloride	17.1	54.0	32.7	0.010	0.398	0.058	16	I
30487-A	Methylene chloride	8.62	55.7	21.0	0.100	0.101	0.100	23	I
30618-A	Methylene chloride	6,580	12,800	9,660	1.00	10.0	3.84	19	I
30487-A	Pyridine	7.75	7.75	7.75	1.0	1.0	1.0	1	I

Table 8-5

(Continued)

Facility-Stream	Pollutant	Influent Conc. (mg/L)			Effluent Conc. (mg/L)			# of Effluent Data Points	Source
		Min.	Max.	Avg.	Min.	Max.	Avg.		
60000-C	Tetrahydrofuran	7,500	8,550	8,340	0.22	2.57	1.54	5	I
30329-B	Toluene	252	252	252	0.124	1.00	0.562	2	I
60000-C	Toluene	515	580	528	0.333	0.630	0.473	5	I
60000-A	Toluene	16.7	21.3	18.6	0.010	0.042	0.022	16	I
60000-B	Toluene	237	668	494	0.010	0.012	0.010	8	I
30487-A	Toluene	15.2	82.6	35.2	0.100	0.100	0.100	23	I

Sources:
I - EPA (List of Analytes) Sampling Program, Reference 3.
R - EPA-Sponsored Alcohol Distillation Study, Reference 10.

Note: Values that were not detected were set at the detection limit.

Table 8-6

Advanced Biological Treatment Performance Data Transfers

Constituent Code	Constituent Name	Kmax Value (a)	BOD_5/ThOD Ratio	Structural Group	Treatment Performance Data Available	Biodegradability Group	Data Transferred From
94	Isopropanol	4.89E-06	54%-83%	alcohol	yes	high	
70	Ethanol	2.45E-06	37%-74%	alcohol	yes	medium	
77	Ethylene glycol		63%	alcohol		high	Ethanol
114	Phenol	2.70E-05	70%	alcohol	yes	high	
29	tert-Butyl alcohol		0.8%	alcohol		medium	Ethanol
97	Methanol (Methyl alcohol)	5.00E-06	51%-75%	alcohol	yes	high	
27	n-Butanol	4.89E-06	33%-58%	alcohol	yes	high	
117	n-Propanol		20%-44%	alcohol		medium	Ethanol
11	Amyl alcohol			alcohol		medium	Ethanol
79	Formaldehyde	1.39E-06	60%	aldehyde	yes	high	
93	Isobutyraldehyde		65.6%	aldehyde		high	Formaldehyde
60	N,N-Dimethylacetamide			amide		low	N,N-Dimethylformamide
80	Formamide			amide		low	N,N-Dimethylformamide
64	N,N-Dimethylformamide	2.70E-06		amide	yes	medium	
99	Methylamine			amine		medium	N,N-Dimethylformamide
55	Diethylamine			amine		medium	N,N-Dimethylformamide
136	Triethylamine			amine	yes	medium	

Table 8-6

(Continued)

Constituent Code	Constituent Name	Kmax Value (a)	BOD_5/ThOD Ratio	Structural Group	Treatment Performance Data Available	Biodegradability Group	Data Transferred From
61	Dimethylamine		64.8%	amine		high	N,N-Dimethylformamide
15	Benzene	5.28E-06	70%	aromatic	yes	high	
12	Aniline	1.97E-06	62%	aromatic		high	Chlorobenzene
62	N,N-Dimethylaniline		9.5%	aromatic		low	2-Methylpyridine
139	Xylenes	8.65E-06		aromatic	yes	high	
106	2-Methylpyridine			aromatic	yes	medium	
35	Chlorobenzene	1.10E-07	1%	aromatic	yes	medium	
124	Pyridine	4.89E-06	52%	aromatic	yes	high	
130	Toluene	2.04E-05	5%-69%	aromatic	yes	high	
48	o-Dichlorobenzene (1,2-Dichlorobenzene)	7.00E-07		aromatic		medium	1,4-Dichlorobenzene
51	1,2-Dichloroethane	5.83E-07	7%	chlorinated alkane	yes	medium	
39	Chloromethane (Methyl chloride)	8.30E-08		chlorinated alkane	yes	low	
134	Trichlorofluoromethane	3.00E-06		chlorinated alkane	yes	medium	
102	Methylene Chloride	6.11E-06		chlorinated alkane	yes	high	
37	Chloroform	8.20E-07	6%	chlorinated alkane	yes	medium	
26	n-Butyl acetate		7%-46%	ester		medium	Isopropyl acetate
71	Ethyl acetate	4.89E-06	16%-68%	ester	yes	high	

Table 8-6

(Continued)

Constituent Code	Constituent Name	Kmax Value (a)	BOD_5/ThOD Ratio	Structural Group	Treatment Performance Data Available	Biodegradability Group	Data Transferred From
95	Isopropyl acetate		12.7%	ester	yes	low	
10	N-Amyl acetate	4.89E-06	38%	ester		high	Ethyl acetate
103	Methyl formate			ester		high	Ethyl acetate
115	Polyethylene glycol 600		0.6%	ether		low	Tetrahydrofuran
67	1,4-Dioxane	4.89E-06		ether	yes	high	
58	Diethyl ether	4.89E-06		ether		high	Tetrahydrofuran
129	Tetrahydrofuran	4.89E-06		ether	yes	high	
96	Isopropyl ether		6.7%	ether		low	Tetrahydrofuran
105	Methyl isobutyl ketone (MIBK)	4.89E-06	4.4%-79%	ketone	yes	high	
118	Acetone	3.61E-07	50%	ketone	yes	high	
25	2-Butanone (MEK)	5.60E-07	46%	ketone	yes	medium	
84	n-Heptane	4.25E-06		alkane	yes	high	
87	n-Hexane	4.25E-06	63%	alkane	yes	high	
43	Cyclohexane	4.25E-06		alkane		high	n-Hexane
113	Petroleum naphtha			alkane			Toluene
3	Acetonitrile	5.00E-06		misc.	yes	high	
101	Methyl cellosolve		7.1%	misc.		low	Ethanol

Table 8-6

(Continued)

Constituent Code	Constituent Name	Kmax Value (a)	BOD_5/ThOD Ratio	Structural Group	Treatment Performance Data Available	Biodegradability Group	Data Transferred From
82	Furfural	4.89E-06	46%	misc.		high	Ethyl acetate
9	Ammonia (aqueous)	2.70E-06		misc.	yes	medium	
66	Dimethyl sulfoxide			misc		low	Chloromethane

(a) Units for Kmax values are (gram constituent/gram biosludge/second)
Kmax values: Reference 18.
BOD_5/ThOD ratios: References 14, 15, 16, and 17).

Table 8-7

Steam Stripping Treatment Performance Data Transfers

Constituent Code	Constituent Name	Henry's Law Constant (atm/gmole/m3)	Source	Structural Group	Transfer Group	Constituent Transferred From
84	N-Heptane	2.85E+00	(a)	n-alkane	high	Methylene chloride
87	N-Hexane	1.55E+00	(a)	n-alkane	high	Methylene chloride
43	Cyclohexane	1.93E-01	(a)	misc.	high	Methylene chloride
134	Trichlorofluoromethane	9.70E-02	(a)	chlorinated alkane	high	Methylene chloride
39	Chloromethane (Methyl chloride)	8.14E-03	(b)	chlorinated alkane	high	Methylene chloride
130	Toluene	5.93E-03	(a)	aromatic	high	Data available
15	Benzene	5.55E-03	(c)	aromatic	high	Methylene chloride
139	Xylenes	5.10E-03	(a)	aromatic	high	Methylene chloride
35	Chlorobenzene	3.93E-03	(b)	aromatic	high	Methylene chloride
37	Chloroform	3.39E-03	(b)	chlorinated alkane	high	Data available
101	Methyl cellosolve	2.90E-03	(a)	misc.	high	Methylene chloride
102	Methylene chloride	2.68E-03	(a)	chlorinated alkane	high	Data available
96	Isopropyl ether	2.24E-03	(c)	ether	medium	Acetone
48	o-Dichlorobenzene (1,2-Dichlorobenzene)	1.94E-03	(b)	aromatic	medium	Acetone
58	Diethyl ether	1.80E-03	(d)	ether	medium	Acetone
51	1,2-Dichloroethane	1.10E-03	(c)	chlorinated alkane	medium	Acetone
26	N-Butyl acetate	4.68E-04	(a)	ester	medium	Acetone

Table 8-7

(Continued)

Constituent Code	Constituent Name	Henry's Law Constant (atm/gmole/m3)	Source	Structural Group	Transfer Group	Constituent Transferred From
10	N-Amyl acetate	3.91E-04	(a)	ester	medium	Acetone
9	Ammonia (aqueous)	3.28E-04	(b)	misc.	medium	Data available
95	Isopropyl acetate	3.17E-04	(e)	ester	medium	Acetone
93	Isobutyraldehyde	1.47E-04	(e)	aldehyde	medium	Acetone
136	Triethylamine	1.38E-04	(a)	amine	medium	Acetone
71	Ethyl acetate	1.20E-04	(c)	ester	medium	Acetone
55	Diethylamine	1.10E-04	(a)	amine	medium	Acetone
129	Tetrahydrofuran	1.10E-04	(f)	ether	medium	Data available
105	MIBK	9.40E-05	(a)	ketone	medium	Acetone
103	Methyl formate	8.10E-05	(g)	ester	medium	Acetone
25	2-Butanone (MEK)	4.36E-05	(b)	ketone	medium	Data available
118	Acetone	3.67E-05	(a)	ketone	medium	Data available
11	Amyl alcohol	2.23E-05	(a)	alcohol	low	Isopropanol
80	Formamide	1.92E-05	(g)	amide	low	Isopropanol
61	Dimethylamine	1.77E-05	(a)	amine	low	Isopropanol
62	N,N-Dimethylaniline	1.75E-05	(a)	aromatic	low	Isopropanol
29	tert-Butyl alcohol	1.17E-05	(a)	alcohol	low	Isopropanol
99	Methylamine	1.11E-05	(a)	amine	low	Isopropanol

Table 8-7

(Continued)

Constituent Code	Constituent Name	Henry's Law Constant (atm/gmole/m3)	Source	Structural Group	Transfer Group	Constituent Transferred From
106	2-Methylpyridine	9.96E-06	(a)	aromatic	low	Isopropanol
82	Furfural	8.11E-06	(e)	misc.	low	Isopropanol
94	Isopropanol	8.07E-06	(a)	alcohol	low	Data available
117	n-Propanol	6.85E-06	(a)	alcohol	low	Ethanol
70	Ethanol	6.26E-06	(a)	alcohol	low	Data available
27	n-Butyl alcohol	5.57E-06	(a)	alcohol	low	Methanol
124	Pyridine	5.30E-06	(g)	aromatic	low	Data available
67	1,4-Dioxane	4.88E-06	(a)	ether	low	Methanol
12	Aniline	2.90E-06	(b,g)	aromatic	low	Methanol
113(i)	Petroleum naphtha	2.70E-06	(g)	misc.	low	Methanol
97	Methanol	2.70E-06	(b)	alcohol	low	Data available
114	Phenol	3.97E-07	(a)	alcohol	not strippable	-
79	Formaldehyde	3.27E-07	(a)	aldehyde	not strippable	-
3	Acetonitrile	2.01E-07	(a)	misc.	not strippable	-
64	N,N-Dimethylformamide	1.29E-07	(g,h)	amide	not strippable	-
115(j)	Polyethylene glycol 600	1.08E-07	(g)	alcohol	not strippable	-
77	Ethylene glycol	1.08E-07	(e)	alcohol	not strippable	-

Table 8-7

(Continued)

Constituent Code	Constituent Name	Henry's Law Constant (atm/gmole/m3)	Source	Structural Group	Transfer Group	Constituent Transferred From
60	N,N-Dimethylacetamide	4.55E-08	(g,h)	amide	not strippable	-
66	Dimethyl sulfoxide	6.00E-09	(g,h)	misc.	not strippable	-

Sources:

(a) EPA Literature Values, Reference 20.
(b) SIMS Model Database, Reference 18.
(c) Alternate EPA Literature Values, References 21, 22, and 23.
(d) UNIFAC Value, Reference 24.
(e) TSDF Air Emission Model, Reference 25.
(f) Toxics Database.
(g) Best Engineering Judgement.
(h) DECHEMA, Reference 26.
(i) Based on best engineering judgement, petroleum naphtha was placed in the "low" strippability group. Its value for Henry's Law Constant was transferred from the constituent with the lowest Henry's Law Constant in the "low" strippability group.
(j) No Henry's Law Constants were found for this constituent; therefore, a Henry's Law Constant was transferred from constituents with similar structures.

Notes:
All values for Henry's Law Constant are at 25°C and 1 atm.
The LTM for constituents without distillation data was transferred from the constituent with the lowest Henry's Law Constant in the transfer group except where noted.
Ammonia data are from air stripping treatment performance.

Table 8-8

Steam Stripping with Distillation Treatment Performance Data Transfers

Constituent Code	Constituent Name	Henry's Law Constant (atm/gmole/m3)	Source	Structural Group	Transfer Group	Constituent Transferred From
84	N-Heptane	2.85E+00	(a)	n-alkane	high	Methylene chloride
87	N-Hexane	1.55E+00	(a)	n-alkane	high	Methylene chloride
43	Cyclohexane	1.93E-01	(a)	misc.	high	Methylene chloride
134	Trichlorofluoromethane	9.70E-02	(a)	chlorinated alkane	high	Methylene chloride
39	Chloromethane (Methyl chloride)	8.14E-03	(b)	chlorinated alkane	high	Methylene chloride
130	Toluene	5.93E-03	(a)	aromatic	high	Data available
15	Benzene	5.55E-03	(c)	aromatic	high	Methylene chloride
139	Xylenes	5.10E-03	(a)	aromatic	high	Methylene chloride
35	Chlorobenzene	3.93E-03	(b)	aromatic	high	Methylene chloride
37	Chloroform	3.39E-03	(b)	chlorinated alkane	high	Data available
101	Methyl cellosolve	2.90E-03	(a)	misc.	high	Methylene chloride
102	Methylene chloride	2.68E-03	(a)	chlorinated alkane	high	Data available
96	Isopropyl ether	2.24E-03	(c)	ether	medium	Acetone
48	o-Dichlorobenzene (1,2-Dichlorobenzene)	1.94E-03	(b)	aromatic	medium	Acetone
58	Diethyl ether	1.80E-03	(d)	ether	medium	Acetone
51	1,2-Dichloroethane	1.10E-03	(c)	chlorinated alkane	medium	Acetone
26	N-Butyl acetate	4.68E-04	(a)	ester	medium	Acetone

Table 8-8

(Continued)

Constituent Code	Constituent Name	Henry's Law Constant (atm/gmole/m3)	Source	Structural Group	Transfer Group	Constituent Transferred From
10	N-Amyl acetate	3.91E-04	(a)	ester	medium	Acetone
9	Ammonia (aqueous)	3.28E-04	(b)	misc.	medium	Data available
95	Isopropyl acetate	3.17E-04	(e)	ester	medium	Acetone
93	Isobutyraldehyde	1.47E-04	(e)	aldehyde	medium	Acetone
136	Triethylamine	1.38E-04	(a)	amine	medium	Acetone
71	Ethyl acetate	1.20E-04	(c)	ester	medium	Acetone
55	Diethylamine	1.10E-04	(a)	amine	medium	Acetone
129	Tetrahydrofuran	1.10E-04	(f)	ether	medium	Data available
105	MIBK	9.40E-05	(a)	ketone	medium	Acetone
103	Methyl formate	8.10E-05	(g)	ester	medium	Acetone
25	2-Butanone (MEK)	4.36E-05	(b)	ketone	medium	Data available
118	Acetone	3.67E-05	(a)	ketone	medium	Data available
11	Amyl alcohol	2.23E-05	(a)	alcohol	low	Methanol
80	Formamide	1.92E-05	(g)	amide	low	Methanol
61	Dimethylamine	1.77E-05	(a)	amine	low	Methanol
62	N,N-Dimethylaniline	1.75E-05	(a)	aromatic	low	Methanol
29	tert-Butyl alcohol	1.17E-05	(a)	alcohol	low	Methanol
99	Methylamine	1.11E-05	(a)	amine	low	Methanol

Table 8-8

(Continued)

Constituent Code	Constituent Name	Henry's Law Constant (atm/gmole/m3)	Source	Structural Group	Transfer Group	Constituent Transferred From
106	2-Methylpyridine	9.96E-06	(a)	aromatic	low	Methanol
82	Furfural	8.11E-06	(e)	misc.	low	Methanol
94	Isopropanol	8.07E-06	(a)	alcohol	low	Methanol
117	n-Propanol	6.85E-06	(a)	alcohol	low	Methanol
70	Ethanol	6.26E-06	(a)	alcohol	low	Methanol
27	n-Butyl alcohol	5.57E-06	(a)	alcohol	low	Methanol
124	Pyridine	5.30E-06	(g)	aromatic	low	Data available
67	1,4-Dioxane	4.88E-06	(a)	ether	low	Methanol
12	Aniline	2.90E-06	(b,g)	aromatic	low	Methanol
113(i)	Petroleum naphtha	2.70E-06	(g)	misc.	low	Methanol
97	Methanol	2.70E-06	(b)	alcohol	low	Data available
114	Phenol	3.97E-07	(a)	alcohol	not strippable	-
79	Formaldehyde	3.27E-07	(a)	aldehyde	not strippable	-
3	Acetonitrile	2.01E-07	(a)	misc.	not strippable	-
64	N,N-Dimethylformamide	1.29E-07	(g,h)	amide	not strippable	-
115(j)	Polyethylene glycol 600	1.08E-07	(g)	alcohol	not strippable	-
77	Ethylene glycol	1.08E-07	(e)	alcohol	not strippable	-

Table 8-8

(Continued)

Constituent Code	Constituent Name	Henry's Law Constant (atm/gmole/m3)	Source	Structural Group	Transfer Group	Constituent Transferred From
60	N,N-Dimethylacetamide	4.55E-08	(g,h)	amide	not strippable	-
66	Dimethyl sulfoxide	6.00E-09	(g,h)	misc.	not strippable	-

Sources:

(a) EPA Literature Values, Reference 20.
(b) SIMS Model Database, Reference 18.
(c) Alternate EPA Literature Values, References 21, 22, and 23.
(d) UNIFAC Value, Reference 24.
(e) TSDF Air Emission Model, Reference 25.
(f) Toxics Database.
(g) Best Engineering Judgement.
(h) DECHEMA, Reference 26.
(i) Based on best engineering judgement, petroleum naphtha was placed in the "low" strippability group. Its value for Henry's Law Constant was transferred from the constituent with the lowest Henry's Law Constant in the "low" strippability group.
(j) No Henry's Law Constants were found for this constituent; therefore, a Henry's Law Constant was transferred from constituents with similar structures.

Notes: All values for Henry's Law Constant are at 25°C and 1 atm.
The LTM for constituents without distillation data was transferred from the constituent with the lowest Henry's Law Constant in the transfer group except where noted.
Ammonia data are from air stripping treatment performance.

Table 8-9

Strippability Groups for Regulated Compounds Established for Assigning Process Design Variables for Steam Stripping with Distillation Technology

Compound/Group	Henry's Law Constant ($atm/gmole/m^3$)
Group 1	
n-Heptane	2.85E+00
n-Hexane	1.55E+00
Group 2	
Cyclohexane	1.93E-01
Trichlorofluoromethane	9.70E-02
Group 3	
Chloromethane (Methyl chloride)	8.14E-03
Toluene	5.93E-03
Benzene	5.55E-03
Xylenes	5.10E-03
Chlorobenzene	3.93E-03
Chloroform	3.39E-03
Methyl cellosolve	2.90E-03
Methylene chloride	2.68E-03
Isopropyl ether	2.24E-03
o-Dichlorobenzene (1,2-Dichlorobenzene)	1.94E-03
Diethyl ether	1.80E-03
1,2-Dichloroethane	1.10E-03
Group 4	
N-Butyl acetate	4.68E-04
N-Amyl acetate	3.91E-04
Ammonia (aqueous)	3.28E-04
Isopropyl acetate	3.17E-04
Isobutyraldehyde	1.47E-04
Triethylamine	1.38E-04
Ethyl acetate	1.20E-04
Diethylamine	1.10E-04
Tetrahydrofuran	1.10E-04
Methyl isobutyl ketone (MIBK)	9.40E-05
Methyl formate	8.10E-05

Table 8-9

(Continued)

Compound/Group	Henry's Law Constant (atm/gmole/m^3)
Group 5	
2-Butanone (MEK)	4.36E-05
Acetone	3.67E-05
Amyl alcohol	2.23E-05
Formamide	1.92E-05
Dimethylamine	1.77E-05
N,N-Dimethylaniline	1.75E-05
tert-Butyl alcohol	1.17E-05
Methylamine	1.11E-05
2-Methylpyridine	9.96E-06
Furfural	8.11E-06
Isopropanol	8.07E-06
n-Propanol	6.85E-06
Ethanol	6.26E-06
n-Butyl alcohol	5.57E-08
Pyridine	5.30E-06
1,4-Dioxane	4.88E-06
Aniline	2.90E-06
Group 6	
Methanol	2.70E-06
Petroleum naphtha	2.70E-06
Group 7	
Phenol	3.97E-07
Formaldehyde	3.27E-07
Acetonitrile	2.01E-07
N,N-Dimethylformamide	1.29E-07
Polyethylene glycol 600	1.08E-07
Ethylene glycol	1.08E-07
N,N-Dimethylacetamide	4.55E-08
Dimethyl sulfoxide	6.00E-09

Table 8-10

Key Process Inputs for Data Transfer Simulations

Strippability Group	Equilibrium Stages Total	Stripping Stages	L/V	V/L
1	4	4	12.0	0.083
2	4	4	12.0	0.083
3	6	4	10.0	0.100
4	10	8	7.5	0.133
5	14	12	4.0	0.250
6	14	12	3.0	0.333

Table 8-11

Secondary Process Inputs for Data Transfer Simulations

Input	Value	Basis
Thermodynamics	Calculated	UNIQUAC/UNIFAC
Mass & Energy Balances	Calculated	Inside/Outside Algorithm by Boston
Steam Pressure	40 psig	Field Test Experience
Column Pressure Drop (includes delta P across condenser)	4 psig	Field Test Experience
Approach for Feed/Effluent HX(a) (Feed temperature of approximately 200°F)	20°F	Field Test Experience

(a) Approach for Feed/Effluent HX is the temperature difference between the inlet bottom temperature and the outlet temperature of the feed to the column.

Table 8-12

Comparison of UNIFAC K-Values and Literature K-Values At 25°C In Water

Chemical	K-Values(a)		Reference
	Estimated with UNIFAC	Literature Values	
Acetone	2.2	2.0	29
Chloroform	221.0	188.	25
Ethanol	0.5	0.3, 1.7	30/29
Isopropyl alcohol	2.1	0.4, 8.3	30/29
Methanol	0.1	0.2, 7.5	30/29
Methylene chloride	140.0	177.2	25
Methyl isobutyl ketone (MIBK)	3.4	2.8, 5.2	30/29
Tetrahydrofuran (THF)	6.4	6.1	30
Toluene	436.7	377.8	18

(a)The K-value of a compound in water at infinite dilution is referred to as the Henry's Law Constant of that compound.

Table 8-13

Simulation Results Supporting Steam Stripping with Distillation Treatment Performance Data Transfers Subcategory A and C Facilities

Compound Strippability Group	Estimated Influent (mg/L)	Estimated Influent is an Industry Average (A)	ASPEN Simulated Effluent(a) (mg/L)	Proposed Long-Term Mean Performance Level (mg/L)
Group 1				
n-Heptane	242	A	<0.005	0.10
n-Hexane	16,600	A (b)	<0.005	0.10
Group 2				
Cyclohexane	467	A	<0.010	0.10
Trichlorofluoromethane	5.8	A	<0.10	0.10
Group 3				
Chloromethane (Methyl chloride)	252	A	<0.050	0.10
Toluene	4,760	A	<0.010	0.10
Benzene	46.2	A	<0.010	0.10
Xylenes	328	A	<0.010	0.10
Chlorobenzene	106	A	<0.010	0.10
Chloroform	257	A	<0.010	0.01
Methylene chloride	3,380	A (b)	<0.010	0.10
Isopropyl ether	19.2	A	<0.050	0.39
1,2-Dichlorobenzene	8.1	A	<0.001	0.39
1,2-Dichloroethane	575	A	<0.010	0.39
Diethyl ether	4,480	A	<0.050	0.39
Group 4				
Tetrahydrofuran	1,820	A	<0.005	1.54
n-Butyl acetate	828	A	<0.500	0.39
n-Amyl acetate	2,870	A	<0.500	0.39
Isopropyl acetate	966	A	<0.500	0.39
Isobutyraldehyde	67.3	A	<0.180	0.39
Triethylamine	3,240	A	<0.050	0.39
Ethyl acetate	16,300	A	<0.500	0.39
Diethylamine	1,440	A	<0.010	0.39
Methyl isobutyl ketone (MIBK)	9,780	A	<0.005	0.39
Methyl formate	276	A	<0.500	0.50

Table 8-13

(Continued)

Compound Strippability Group	Estimated Influent (mg/L)	Estimated Influent is an Industry Average (A)	ASPEN Simulated Effluent(a) (mg/L)	Proposed Long-Term Mean Performance Level (mg/L)
Group 5				
Pyridine	1,110	A	0.247	1.00
2-Butanone	262	A	<0.050	25.8
Acetone	3,680	A	<0.050	0.39
Amyl alcohol	486	A	<0.500	1.52
Dimethylamine	9,990	A	<0.050	1.52
N,N-Dimethylaniline	1,670	A	<0.050	1.52
tert-Butyl alcohol	254	A	<0.500	1.52
Methylamine	4,030	A	<0.050	1.52
2-Methylpyridine	45.1	A	<0.050	1.52
Furfural	0.7	A	0.115	1.52
Isopropanol	3,190	A	<0.050	1.52
n-Propanol	261	A	<0.050	1.52
Ethanol	28,900	A	0.697	1.52
n-Butyl alcohol	37,900	A	0.159	1.52
1,4-Dioxane	180	A	<0.050	1.52
Aniline	22.8	A	<0.010	1.52
Group 6				
Methanol	20,000	(c)	1.040	1.52

(a) The < sign indicates estimated concentration is below detection limit.
(b) Simulated with concentration at solubility limit.
(c) Approximate concentration during field test.

Note: Simulations were not run for methyl cellosolve, formamide, and petroleum naphtha, since appropriate physical property data were not available.

Table 8-14

Simulation Results Supporting Steam Stripping with Distillation Treatment Performance Data Transfers Subcategory B and D Facilities

Compound/Group	Estimated Influent (mg/L)	Estimated Influent is an Industry Average (A)	ASPEN Simulated Effluent(a) (mg/L)	Proposed Long-Term Mean Performance Level (mg/L)
Group 1				
n-Hexane	423	A	<0.005	0.10
Group 2				
Trichlorofluoromethane	185	A	<0.10	0.10
Group 3				
Toluene	66.1	A	<0.010	0.10
Chloroform	7.8	A	<0.010	0.01
Methylene chloride	3,380	A (b)	<0.010	0.10
Isopropyl ether	28.3	A	<0.050	0.10
Diethyl ether	0.7	A	<0.050	0.10
Group 4				
N-Amyl acetate	400	A	<0.500	0.39
Isopropyl acetate	110	A	<0.500	0.39
Triethylamine	<0.1	A	<0.050	0.39
Ethyl acetate	1,070	A	<0.500	0.39
Group 5				
Pyridine	45.0	A	0.2	1.00
Acetone	42,700	A	<0.050	0.39
Isopropanol	2,650	A	<0.050	1.52
Ethanol	2,920	A	0.7	1.52
n-Butyl alcohol	7.3	A	0.2	1.52
Group 6				
Methanol	20,000	(b)	1.0	1.52

(a) The < sign indicates estimated concentration is below detection limit.
(b) Simulated with concentration at solubility limit.
(c) Approximate concentration during field test.

Note: Simulations were run for those regulated constituents with raw loads reported in the Detailed Questionnaire.

Table 8-15

Long-Term Mean Concentrations of BOD_5, COD, and TSS for Each Regulatory Option

Regulatory Option	Subcategory/Discharge Status	Long-Term Mean Concentration (mg/L)		
		BOD_5	COD	TSS
BPT Option 2	A and C / Direct	42.2	486.9	79.4
BPT Option 3	A and C / Direct	42.2	486.9	42.9
BPT Option 4	A and C / Direct	42.2	486.9	33.4
BPT Option 5	A and C / Direct	42.2	486.9	11.9
BCT Option 2	A and C / Direct	42.2	-	79.4
BCT Option 3	A and C / Direct	42.2	-	42.9
BCT Option 4	A and C / Direct	42.2	-	33.4
BCT Option 5	A and C / Direct	42.2	-	11.9
BAT Option 1	A and C / Direct	-	486.9	-
BAT Option 2	A and C / Direct	-	486.9	-
BAT Option 3	A and C / Direct	-	486.9	-
BAT Option 4	A and C / Direct	-	204.5	-
NSPS Option 1	A and C / Direct	20.1	416.0	30.4
NSPS Option 2	A and C / Direct	20.1	174.7	30.4
BPT Option 2	B and D / Direct	7.2	44.3	18.1
BPT Option 3	B and D / Direct	7.2	44.3	6.2
BCT Option 2	B and D / Direct	7.2	-	18.1
BCT Option 3	B and D / Direct	7.2	-	6.2
BAT Option 1	B and D / Direct	-	44.3	-
BAT Option 2	B and D / Direct	-	44.3	-
BAT Option 3	B and D / Direct	-	44.3	-
BAT Option 4	B and D / Direct	-	18.6	-
NSPS Option 1	B and D / Direct	6.4	17.1	7.7
NSPS Option 2	B and D / Direct	6.4	7.2	7.7

Table 8-16

Long-Term Mean Treatment Performance Concentrations for Priority and Nonconventional Pollutants with Available Treatment Performance Data

Pollutant Code	Pollutant	Long-Term Mean Concentration (mg/L)		
		Adv. Biological Treatment	Steam Stripping	Steam Stripping with Distillation
003	Acetonitrile	0.005	-	-
015	Benzene	0.010	-	-
025	2-Butanone (MEK)	0.051	121	25.8
027	n-Butyl alcohol	0.250	-	-
035	Chlorobenzene	0.010	-	-
037	Chloroform	0.010	0.010	0.010
039	Chloromethane (Methyl chloride)	0.052	-	-
051	1,2-Dichloroethane	0.064	-	-
064	N,N-Dimethylformamide	0.011	-	-
067	1,4-Dioxane	0.055	-	-
070	Ethanol	1.00	351	-
071	Ethyl acetate	0.755	-	-
079	Formaldehyde	0.343	-	-
084	n-Heptane	0.005	-	-
087	n-Hexane	0.005	-	-
094	Isopropanol	0.281	76.3	-
095	Isopropyl acetate	0.500	-	-
097	Methanol	1.00	1,370	1.52
102	Methylene chloride	0.089	0.100	0.100
105	Methyl isobutyl ketone (MIBK)	0.030	-	-
106	2-Methylpyridine	0.050	-	-
114	Phenol	0.010	-	-
118	Acetone	0.113	3.00	0.389

Table 8-16

(Continued)

Pollutant Code	Pollutant	Long-Term Mean Concentration (mg/L)		
		Adv. Biological Treatment	Steam Stripping	Steam Stripping with Distillation
124	Pyridine	0.010	1.00	1.00
129	Tetrahydrofuran	1.22	1.54	1.54
130	Toluene	0.010	0.100	0.100
134	Trichlorofluoromethane	0.219	-	-
136	Triethylamine	0.050	-	-
139	Xylenes	0.010	-	-

A dash indicates treatment performance data for a specific technology is not available.

Table 8-17

Long-Term Mean Treatment Performance Concentrations for Priority and Nonconventional Pollutants (Including Treatment Performance Data Transfers)

Pollutant Code	Pollutant	Long-Term Mean Concentration (mg/L)		
		Advanced Biological Treatment	Steam Stripping	Steam Stripping with Distillation
003	Acetonitrile	0.005	NS	NS
009	Ammonia (aqueous)	2.56	9.91	9.91
010	n-Amyl acetate	0.755	3.00	0.389
011	Amyl alcohol	1.00	76.3	1.52
012	Aniline	0.010	1,370	1.52
015	Benzene	0.010	0.100	0.100
025	2-Butanone (MEK)	0.051	121	25.8
026	n-Butyl acetate	0.50	3.00	0.389
027	n-Butyl alcohol	0.250	1,370	1.52
029	tert-Butyl alcohol	1.00	76.3	1.52
035	Chlorobenzene	0.010	0.100	0.100
037	Chloroform	0.010	0.010	0.010
039	Chloromethane (Methyl chloride)	0.052	0.100	0.100
043	Cyclohexane	0.005	0.100	0.100
048	o-Dichlorobenzene (1,2-Dichlorobenzene)	0.001	3.00	0.389
051	1,2-Dichloroethane	0.064	3.00	0.389
055	Diethylamine	0.011	3.00	0.389
058	Diethyl ether	1.22	3.00	0.389
060	N,N-Dimethylacetamide	0.011	NS	NS
061	Dimethylamine	0.011	76.3	1.52
062	N,N-Dimethylaniline	0.050	76.3	1.52

Table 8-17

(Continued)

Pollutant Code	Pollutant	Long-Term Mean Concentration (mg/L)		
		Advanced Biological Treatment	Steam Stripping	Steam Stripping with Distillation
064	N,N-Dimethylformamide	0.011	NS	NS
066	Dimethyl sulfoxide	0.052	NS	NS
067	1,4-Dioxane	0.055	1,370	1.52
070	Ethanol	1.00	351	1.52
071	Ethyl acetate	0.755	3.00	0.389
077	Ethylene glycol	1.00	NS	NS
079	Formaldehyde	0.343	NS	NS
080	Formamide	0.011	76.3	1.52
082	Furfural	0.755	76.3	1.52
084	n-Heptane	0.005	0.100	0.100
087	n-Hexane	0.005	0.100	0.100
093	Isobutyraldehyde	0.343	3.00	0.389
094	Isopropanol	0.281	76.3	1.52
095	Isopropyl acetate	0.500	3.00	0.389
096	Isopropyl ether	1.22	3.00	0.389
097	Methanol	1.00	1,370	1.52
099	Methylamine	0.011	76.3	1.52
101	Methyl cellosolve	1.00	0.100	0.100
102	Methylene chloride	0.089	0.100	0.100
103	Methyl formate	0.755	3.00	0.389
105	Methyl isobutyl ketone (MIBK)	0.030	3.00	0.389
106	2-Methylpyridine	0.050	76.3	1.52
113	Petroleum naphtha	0.010	1,370	1.52
114	Phenol	0.010	NS	NS

Table 8-17

(Continued)

Pollutant Code	Pollutant	Long-Term Mean Concentration (mg/L)		
		Advanced Biological Treatment	Steam Stripping	Steam Stripping with Distillation
115	Polyethylene glycol 600	1.22	NS	NS
117	n-Propanol	1.00	351	1.52
118	Acetone	0.113	3.00	0.389
124	Pyridine	0.010	1.00	1.00
129	Tetrahydrofuran	1.22	1.54	1.54
130	Toluene	0.010	0.100	0.100
134	Trichlorofluoromethane	0.219	0.100	0.100
136	Triethylamine	0.050	3.00	0.389
139	Xylenes	0.010	0.100	0.100

NS - Constituent is not strippable.

Table 8-18

Long-Term Mean Treatment Performance Concentrations for Priority and Nonconventional Pollutants for the Steam Stripping Followed by Advanced Biological Treatment Train

Pollutant Code	Pollutant	Long-Term Mean Concentration (mg/L)
003	Acetonitrile	0.005
009	Ammonia (aqueous)	2.56
010	n-Amyl acetate	0.026
011	Amyl alcohol	0.168
012	Aniline	2.20
015	Benzene	0.010
025	2-Butanone (MEK)	0.170
026	n-Butyl acetate	0.022
027	n-Butyl alcohol	3.30
029	tert-Butyl alcohol	0.168
035	Chlorobenzene	0.0002
037	Chloroform	0.00001
039	Chloromethane (Methyl chloride)	0.001
043	Cyclohexane	0.001
048	o-Dichlorobenzene (1,2-Dichlorobenzene)	0.010
051	1,2-Dichloroethane	0.015
055	Diethylamine	0.0006
058	Diethyl ether	0.144
060	N,N-Dimethylacetamide	0.011
061	Dimethylamine	0.015
062	N,N-Dimethylaniline	1.35
064	N,N-Dimethylformamide	0.011
066	Dimethyl sulfoxide	0.052
067	1,4-Dioxane	1.37
070	Ethanol	0.772
071	Ethyl acetate	0.026
077	Ethylene glycol	1.00

Table 8-18

(Continued)

Pollutant Code	Pollutant	Long-Term Mean Concentration (mg/L)
079	Formaldehyde	0.343
080	Formamide	0.015
082	Furfural	0.671
084	n-Heptane	0.0005
087	n-Hexane	0.001
093	Isobutyraldehyde	0.589
094	Isopropanol	0.200
095	Isopropyl acetate	0.022
096	Isopropyl ether	0.144
097	Methanol	0.412
099	Methylamine	0.015
101	Methyl cellosolve	0.0002
102	Methylene chloride	0.010
103	Methyl formate	0.026
105	Methyl isobutyl ketone (MIBK)	0.010
106	2-Methylpyridine	1.35
113	Petroleum naphtha	0.010
114	Phenol	0.010
115	Polyethylene glycol 600	1.22
117	n-Propanol	0.772
118	Acetone	0.050
124	Pyridine	0.006
129	Tetrahydrofuran	0.074
130	Toluene	0.010
134	Trichlorofluoromethane	0.001
136	Triethylamine	50.0
139	Xylenes	0.0002

Table 8-19

Long-Term Mean Treatment Performance Concentrations for Priority and Nonconventional Pollutants for the Steam Stripping with Distillation Followed by Advanced Biological Treatment Train

Pollutant Code	Pollutant	Long-Term Mean Concentration (mg/L)
003	Acetonitrile	0.005
009	Ammonia (aqueous)	2.56
010	n-Amyl acetate	0.003
011	Amyl alcohol	0.003
012	Aniline	0.002
015	Benzene	0.010
025	2-Butanone (MEK)	0.036
026	n-Butyl acetate	0.003
027	n-Butyl alcohol	0.004
029	tert-Butyl alcohol	0.003
035	Chlorobenzene	0.0002
037	Chloroform	0.00001
039	Chloromethane (Methyl chloride)	0.001
043	Cyclohexane	0.001
048	o-Dichlorobenzene (1,2-Dichlorobenzene)	0.010
051	1,2-Dichloroethane	0.002
055	Diethylamine	0.0001
058	Diethyl ether	0.019
060	N,N-Dimethylacetamide	0.011
061	Dimethylamine	0.0003
062	N,N-Dimethylaniline	0.027
064	N,N-Dimethylformamide	0.011
066	Dimethyl sulfoxide	0.052
067	1,4-Dioxane	0.002
070	Ethanol	0.003
071	Ethyl acetate	0.003
077	Ethylene glycol	1.00
079	Formaldehyde	0.343

Table 8-19

(Continued)

Pollutant Code	Pollutant	Long-Term Mean Concentration (mg/L)
080	Formamide	0.0003
082	Furfural	0.013
084	n-Heptane	0.0005
087	n-Hexane	0.001
093	Isobutyraldehyde	0.076
094	Isopropanol	0.200
095	Isopropyl acetate	0.003
096	Isopropyl ether	0.019
097	Methanol	0.0004
099	Methylamine	0.0003
101	Methyl cellosolve	0.0002
102	Methylene chloride	0.010
103	Methyl formate	0.003
105	Methyl isobutyl ketone (MIBK)	0.010
106	2-Methylpyridine	0.027
113	Petroleum naphtha	0.010
114	Phenol	0.010
115	Polyethylene glycol 600	1.22
117	n-Propanol	0.003
118	Acetone	0.050
124	Pyridine	0.006
129	Tetrahydrofuran	0.074
130	Toluene	0.010
134	Trichlorofluoromethane	0.001
136	Triethylamine	50.0
139	Xylenes	0.0002

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SECTION 9

POLLUTANT REDUCTION ESTIMATES

9.1 Introduction

EPA obtained data on pollutant loads generated by pharmaceutical manufacturing processes and the ultimate fate of these loads through the Detailed Questionnaire. Using these data and the treatment performance data presented in Section 8, the Agency has developed estimates of untreated and current, pollutant discharge loads from the pharmaceutical manufacturing industry. The Agency also calculated the pollutant discharge loads that would remain after implementation of each of the regulatory options considered.

The following information is presented in this section:

- Section 9.2 presents the estimated untreated loads of pollutants in process wastewaters based on responses to the Detailed Questionnaire;
- Section 9.3 presents the loads of pollutants currently being discharged based on responses to the Detailed Questionnaire;
- Section 9.4 discusses estimated end-of-pipe discharge loads for each regulatory option; and
- Section 9.5 discusses the pollutant load reductions expected through steam stripping, steam stripping with distillation, advanced biological treatment, and granular activated carbon treatment.

9.2 Untreated Loads

The Agency estimated untreated loads, by pollutant, which are generated by pharmaceutical manufacturing processes based on responses to the Detailed

Questionnaire. The untreated load was estimated as the sum of the discharge load, air emissions from wastewater load, and degraded/destroyed load. These loads from the detailed questionnaire for each facility were summed by pollutant across all facilities within a subcategory group. Table 9-1 lists the estimated untreated loads for each pollutant by Subcategory and type of discharge.

The untreated loads for the Subcategory D indirect dischargers were scaled up according to the methodology discussed in Section 3.2.3 and presented in Reference (1). This scale-up was used to estimate the total amount of pollutants for all Subcategory D indirect dischargers, including the facilities which were not sent a Detailed Questionnaire. The table below summarizes the total amount of pollutant load in untreated wastewater from Subcategory B and D indirect dischargers.

	Subcategory B and D Indirect Dischargers from the Detailed Questionnaire	Subcategory D Indirect Dischargers Without Questionnaire (Estimate)	Total Subcategory B and D Indirect Dischargers (Estimate)
Total Raw Load for Priority and Nonconventional Pollutants (lbs/yr)	6,990,000	193,000	7,180,000

9.3 Current Baseline Loads

The current baseline loads are those loads, by pollutant, which are currently discharged by pharmaceutical manufacturing processes to a POTW or to surface water based on responses to the Detailed Questionnaire. Those discharge loads available from the Detailed Questionnaire for each facility were summed by pollutant across all facilities within a subcategory group. Table 9-2 lists the current baseline loads for each pollutant by subcategory group and type of discharge.

The current baseline loads for the Subcategory D indirect dischargers were scaled up according to the methodology discussed in Section 3.2.3 and presented in Reference [1].

This scale-up was used to estimate the total amount of pollutants for all Subcategory D indirect dischargers, including the facilities which were not sent a Detailed Questionnaire. The table below summarizes the total amount of pollutants currently discharged by Subcategory B and D indirect dischargers.

	Subcategory B and D Indirect Dischargers from the Detailed Questionnaire	Subcategory D Indirect Dischargers Without Questionnaire (estimate)	Total Subcategory B and D Indirect Dischargers (estimate)
Total Current Baseline Loads for Priority and Nonconventional Pollutants (lbs/yr)	1,610,000	460,000	2,070,000

9.4 End-of-Pipe Discharge Loads for Each Regulatory Option

End-of-pipe discharge loads for the proposed BPT, BAT, and PSES regulatory options are presented by subcategory and pollutant in this section. (Because EPA proposes to establish BCT equal to BPT, the discharge loads based on the proposed BCT technology would be identical to those based on the proposed BPT technology). These loads were calculated in the following manner. For each facility, current discharge loads were converted to an estimated current effluent concentration using the pollutant discharge load, facility process wastewater flow, and a conversion factor. For each facility, current estimated effluent concentrations were then compared to the long term mean concentrations at the end of the treatment train for a particular regulatory option. The lower of these concentrations was used along with the facility flow and an appropriate conversion factor to determine facility specific end-of-pipe discharge loads [23]. Loads from all facilities within a subcategory group were then summed to provide the subcategory-wide estimates.

9.4.1 BPT

The regulatory options under BPT address the loads and concentrations of BOD_5, TSS, COD, and cyanide. There are five regulatory options considered under BPT for Subcategory A and/or C direct discharger facilities and three regulatory options considered under BPT for Subcategory B and/or D direct discharger facilities. Indirect dischargers are not regulated under BPT.

The regulatory options considered under BPT for Subcategory A and/or C direct discharger facilities are: 1) current cyanide destruction followed by current (in-place) biological treatment; 2) in-plant cyanide destruction, followed by end-of-pipe advanced biological treatment; 3) in-plant cyanide destruction, followed by end-of-pipe advanced biological treatment and effluent filtration; 4) in-plant cyanide destruction, followed by end-of-pipe advanced biological treatment and polishing pond treatment; and 5) in-plant cyanide destruction, followed by end-of-pipe advanced biological treatment, effluent filtration, and polishing pond treatment. Estimated end-of-pipe discharge loads for each of these options are presented below.

	Subcategory A and C BPT Discharge Loads (lbs/yr)				
Pollutant	**Option 1**	**Option 2**	**Option 3**	**Option 4**	**Option 5**
BOD_5	3,260,000	2,330,000	2,330,000	2,330,000	2,330,000
COD	31,700,000	21,800,000	21,800,000	21,800,000	21,800,000
TSS	6,330,000	4,180,000	3,170,000	2,590,000	1,020,000
Cyanide	45	7	7	7	7

The regulatory options considered under BPT for Subcategory B and D direct discharger facilities are: 1) current (in-place) biological treatment; 2) end-of-pipe advanced biological treatment; and 3) end-of-pipe advanced biological treatment and effluent filtration. Because no cyanide is discharged at Subcategory B and D facilities, cyanide

destruction is not included as part of the technology basis for these subcategories. Estimated end-of-pipe discharge loads for each of these options are presented below.

Pollutant	Subcategory B and D BPT Discharge Loads (lbs/yr)		
	Option 1	Option 2	Option 3
BOD_5	57,500	47,400	47,400
COD	294,000	234,000	234,000
TSS	82,400	77,600	46,600

Because Option 1 for the four manufacturing subcategories represents current treatment at facilities, the discharge loads corresponding to that option in the tables above represents current discharge loads. Treatment with filtration and/or polishing ponds after advanced biological treatment will reduce TSS concentrations in wastewater, as reflected in the estimated TSS discharge loads. However, the Agency assumed that no additional reduction in BOD_5 and COD would occur as a result of filtration or settling in polishing ponds.

9.4.2 BAT

The regulatory options considered under BAT address the loads and concentrations of priority and nonconventional pollutants, including ammonia and cyanide where appropriate. There are four regulatory options considered under BAT for Subcategory A and C and B and D direct discharger facilities.

The regulatory options considered under BAT for Subcategory A and C direct discharging facilities are: 1) in-plant cyanide destruction, followed by end-of-pipe advanced biological treatment with nitrification; 2) in-plant steam stripping and cyanide destruction, followed by end-of-pipe advanced biological treatment; 3) in-plant steam stripping with distillation and cyanide destruction, followed by end-of-pipe advanced

biological treatment; and 4) in-plant steam stripping with distillation and cyanide destruction, followed by end-of-pipe advanced biological treatment and granular activated carbon adsorption (GAC). Table 9-3 presents estimated end-of-pipe discharge loads for each of these options.

The regulatory options under BAT for Subcategory B and D direct discharging facilities are the same as those for the Subcategory A and C direct discharging facilities with the exception of cyanide destruction. Because no cyanide is discharged at Subcategory B and D facilities, cyanide destruction is not included as part of the technology basis for these subcategories. For the same reason, treatment technologies specific to ammonia (i.e., nitrification) are also excluded. Table 9-4 presents estimated end-of-pipe discharge loads for each of the regulatory options under BAT for B and D direct discharging facilities.

It should be noted that for certain organic pollutants that are either not strippable or are present at concentrations below the minimum analytical level, there is no apparent end-of-pipe wastewater load reduction between Options 1 and 2. Additionally, all regulated organic pollutants amenable to granular activated carbon (GAC) treatment will be at or below the minimum analytical level after Option 3. Therefore, no additional load reduction is apparent between Options 3 and 4. GAC will achieve additional load removal of COD (and the organics that make up the COD), as demonstrated in the load reduction tables in Section 9.5.2.

9.4.3 PSES

The regulatory options considered under PSES address the loads and concentrations of priority and nonconventional organic pollutants, and, where appropriate, ammonia and cyanide. There are four regulatory options considered under PSES for Subcategory A and C indirect discharging facilities and three regulatory options considered under PSES

for Subcategory B and D indirect discharging facilities. Direct dischargers are not regulated under PSES.

The regulatory options considered under PSES for Subcategory A and C indirect discharging facilities are: 1) in-plant steam stripping and cyanide destruction; 2) in-plant steam stripping with distillation and cyanide destruction; 3) in-plant steam stripping with distillation and cyanide destruction, followed by end-of-pipe advanced biological treatment; and 4) in-plant steam stripping with distillation and cyanide destruction, followed by end-of-pipe advanced biological treatment and granular activated carbon adsorption. Table 9-5 presents estimated end-of-pipe discharge loads for each of these options.

The regulatory options considered under PSES for Subcategory B and D indirect discharging facilities are: 1) in-plant steam stripping; 2) in-plant steam stripping with distillation; and 3) in-plant steam stripping with distillation, followed by granular activated carbon adsorption. Because no cyanide is discharged at Subcategory B and D facilities, cyanide destruction is not included as part of the technology basis for these subcategories. Table 9-6 presents estimated end-of-pipe discharge loads for each of these options.

The end-of-pipe loads for the Subcategory D indirect discharging facilities were also scaled up according to the methodology discussed in Section 3.2.3 and in Reference (1). An estimate of the total end-of-pipe discharge loads for the Subcategory D indirect discharging facilities including those not sent a Detailed Questionnaire are presented in the table below.

	Subcategory B and D Indirect Dischargers With the Detailed Questionnaire	Subcategory D Indirect Dischargers Without Questionnaire (estimate)	Total Subcategory B and D Indirect Dischargers (estimate)
Total Priority and Nonconventional Pollutant PSES Option 1 Loads (lbs/yr)	551,000	144,000	695,000
Total Priority and Nonconventional Pollutant PSES Option 2 Loads (lbs/yr)	28,800	1,610	30,400
Total Priority and Nonconventional Pollutant PSES Option 3 Loads (lbs/yr)	28,600	1,590	30,200

Certain organic pollutants that are either not strippable, or are present at concentrations below the minimum analytical level, will not have loads different from current baseline loads under Option 1 for PSES. Additionally, all regulated organic pollutants at Subcategory A and C facilities amenable to GAC treatment will be at or below the minimum analytical level after Option 2. Therefore, no additional load reduction of regulated organic pollutants is apparent between Options 2 and 3 for Subcategory A and C indirect discharging facilities. GAC will, however, achieve additional load removal of COD at these facilities, as demonstrated in the load reduction tables in Section 9.4.3. Subcategory B and D indirect discharging facilities will achieve load reductions through GAC for a few of the regulated organic pollutants, as well as COD.

9.5 Pollutant Load Reduction Estimates

Each regulatory option considered consists of a treatment train of technology components. The set of options considered for each regulation in each subcategory is generally a series, where each option builds upon a prior option by adding a technology component to the treatment train. For example, BAT Option 1 for Subcategory A and C facilities includes cyanide destruction and advanced biological treatment with nitrification. BAT Option 2 adds in-plant steam stripping to the treatment train. Load reductions through each regulatory option are discussed in this section. In some cases,

the addition of one treatment technology (e.g., steam stripping) may obviate the need for a technology that had been part of a prior option (e.g., nitrification).

A cyanide destruction unit is included in every BPT, BAT, and PSES regulatory option for Subcategories A and C. All load reductions for cyanide are through the cyanide destruction unit. Therefore, no additional load reductions for cyanide are shown in options beyond Option 1.

9.5.1 BPT

Load reductions through the cyanide destruction units are 38 lbs of cyanide/yr for Subcategory A and C facilities regulated under BPT. These load reductions correspond to the load reduction between current baseline loads and end-of-pipe discharge loads for BPT Option 1.

Load reductions through advanced biological treatment for BOD_5, TSS, and COD are shown below. These load reductions correspond to the load reduction between BPT Options 1 and 2.

Pollutant	Load Reduction through Advanced Biological Treatment for Subcategory A and C Direct Dischargers (lbs/yr)	Load Reduction through Advanced Biological Treatment for Subcategory B and D Direct Dischargers (lbs/yr)
BOD_5	931,000	10,000
COD	9,840,000	59,600
TSS	2,150,000	4,820

TSS loads can be further reduced by adding effluent filtration, polishing ponds, or both effluent filtration and polishing ponds. Load reductions through effluent filtration are shown below. These load reductions correspond to the load reductions between BPT Options 2 and 3.

Pollutant	Load Reduction through Filtration for Subcategory A and C Direct Dischargers (lbs/yr)	Load Reduction through Filtration for Subcategory B and D Direct Dischargers (lbs/yr)
TSS	1,010,000	31,000

The load reductions through polishing ponds are shown below. These load reductions correspond to the load reductions between BPT Options 2 and 4.

Pollutant	Load Reduction through Polishing Ponds for Subcategory A and C Direct Dischargers (lbs/yr)
TSS	1,590,000

The load reductions through effluent filtration followed by polishing ponds are shown below. These load reductions correspond to the load reductions between BPT Options 2 and 5.

Pollutant	Load Reduction Through Effluent Filtration Followed by Polishing Ponds for A and C Direct Dischargers (lbs/yr)
TSS	3,160,000

9.5.2 BAT

Table 9-7 presents load reductions through end-of-pipe advanced biological treatment with nitrification for organic pollutants and ammonia under BAT Option 1. These load reductions correspond to the load reduction between current baseline loads and BAT Option 1 loads for both A and C and B and D direct dischargers.

Table 9-8 presents load reductions through in-plant steam stripping followed by end-of-pipe advanced biological treatment for organic pollutants and, for Subcategories A and C, ammonia under BAT Option 2. Table 9-9 presents load reductions through in-plant steam stripping with distillation followed by end-of-pipe advanced biological treatment for organic pollutants and, for Subcategories A and C, ammonia under BAT Option 3. These load reductions were developed from each facility's current baseline loads to their proposed load under the regulatory option. In addition, credit was given for steam stripper or distillation removal of pollutant loads that are estimated as current air emissions from wastewater.

Current air emissions were estimated by the Agency using the WATER7 model, discussed in detail in Section 12.3. The WATER7 model was used to predict the disposal pathways (i.e., degraded, discharged, or emitted to air) of the organic pollutants present in untreated pharmaceutical manufacturing wastewaters. The Agency found that the WATER7 model calculated a greater percentage of wastewater organic constituents emitted to the air than most facilities reported in the Detailed Questionnaire, and that these air emissions were most likely to occur in open equalization or neutralization units with mixing in the wastewater treatment system, downstream of any in-plant steam stripping or distillation unit. For this reason, the pollutant load reductions shown for BAT Options 2 and 3 include these captured air emissions, in addition to the reduction to the current end-of-pipe wastewater discharge loads.

For BAT Option 4, the Agency estimated the COD load reduction through treatment by granular activated carbon adsorption. The Agency estimated that there will be no measurable additional load reduction of specific regulated organic constituents through GAC beyond the level of treatment provided by in-plant steam stripping with distillation followed by advanced biological treatment. The COD load reduction expected under BAT Option 4 for Subcategory A and C and B and D facilities is presented in the table below.

COD Load Reduction Through GAC at A and C Facilities (lbs/yr)	COD Load Reduction Through GAC at B and D Facilities (lbs/yr)
4,750,000	451,000

9.5.3 PSES

As discussed in more detail in Section 17 of this document, EPA makes two alternative proposals concerning the establishment of PSES for the four manufacturing subcategories. The following discussion corresponds to co-proposal (1), which would regulate 45 priority and nonconventional pollutants of concern, and ammonia and cyanide for Subcategories A and C. Co-proposal (2) would regulate 12 priority and nonconventional pollutants of concern, and ammonia and cyanide for Subcategories A and C. Load reductions achieved under co-proposal (2) are represented in Tables 9-10, 9-11, and 9-12 by asterisks, which identify the pollutants that would be regulated under that co-proposal.

Table 9-10 presents load reductions through in-plant steam stripping for priority and nonconventional pollutants under PSES Option 1. Table 9-11 presents load reductions through in-plant steam stripping with distillation for priority and nonconventional pollutants under PSES Option 2. These load reductions were developed based on the difference between each facility's current baseline loads and the estimated load under the regulatory option. In addition, because steam stripping and distillation technology reduce downstream air emissions from wastewater, credit was given for pollutant loads that are currently emitted to air that would be captured by these technologies.

Load reductions for the Subcategory D indirect dischargers were also scaled up according to the methodology discussed in Section 3.2.3 and presented in Reference (1). An estimate of the total load reductions for the Subcategory D indirect dischargers including those not sent a Detailed Questionnaire are presented in the table below.

	Subcategory B and D Indirect Dischargers from the Detailed Questionnaire	Subcategory D Indirect Dischargers Without Questionnaire (estimate)	Total Subcategory B and D Indirect Dischargers (estimates)
Total Load Reduction Through Steam Stripping (lbs/yr)	4,130,000	323,000	4,560,000
Total Load Reduction Through Distillation (lbs/yr)	4,660,000	464,000	5,120,000

Table 9-12 presents load reductions through in-plant steam stripping with distillation followed by end-of-pipe advanced biological treatment for organic pollutants and ammonia under PSES Option 3 for Subcategory A and C indirect dischargers. These load reductions were calculated based on the difference between each facility's current baseline loads and their estimated load under the regulatory option. Similar to Option 2, credit was also given for removal of pollutant loads that are estimated as current air emissions that would be captured by in-plant steam strippers and distillation columns. There is no option for Subcategory B and D indirect dischargers that includes advanced biological treatment.

For PSES Option 4 for Subcategory A and C indirect dischargers, the Agency estimated COD load reduction through granular activated carbon treatment. The Agency estimates that there will be no measurable additional load reduction of specific regulated organic constituents through carbon treatment beyond the level of treatment provided by in-plant steam stripping with distillation followed by advanced biological treatment. For PSES Option 3 for Subcategory B and D indirect dischargers, the Agency estimated COD load reduction through granular activated carbon treatment, as well as the load reduction of a few regulated organic constituents amenable to activated carbon treatment after in-plant steam stripping with distillation. The COD load reduction and the load reduction of the affected regulated organics expected through granular activated carbon treatment is presented in the table below. Load reductions for Subcategory B and D facilities based

on Detailed Questionnaire responses, as well as scaled-up to the entire industry are presented.

	Subcategory A and C Indirect Dischargers	Subcategory B and D Indirect Dischargers from the Detailed Questionnaire	Total Subcategory B and D Indirect Dischargers (estimate with scale-up)
COD Load Reduction Through GAC (lbs/yr)	4,910,000	2,840,000	3,570,000
Total Organic Pollutant Load Reduction Through GAC (lbs/yr)	0	194	213

Table 9-1

Estimated Untreated Pollutant Loads by Subcategory Group and Discharge Mode (lbs/yr)

Pollutant	A and C Direct Dischargers	B and D Direct Dischargers	A and C Indirect Dischargers	B and D Indirect Dischargers
Conventionals and COD				
BOD_5	77,026,379	1,309,631	NA	NA
COD	170,414,438	2,454,864	NA	NA
TSS	23,383,184	565,057	NA	NA
Priority Organics				
Benzene	1,700	0	121,400	0
Chlorobenzene	10,959	0	84,710	0
Chloroform	402,005	0	488,980	77
Chloromethane (Methyl chloride)	194,604	0	5,148	0
o-Dichlorobenzene (1,2-Dichlorobenzene)	0	0	21,499	0
1,2-Dichloroethane	586,115	0	6,552	0
Methylene chloride	8,074,997	25	7,170,355	780,865
Phenol	364,720	1,811	6,693	714
Toluene	3,632,402	0	2,964,688	2,276
Priority Organics Subtotal	**13,267,502**	**1,836**	**10,870,025**	**783,932**
Cyanide	41,733	0	75,065	0
Priority Pollutant Total	**13,309,235**	**1,836**	**10,945,090**	**783,932** (a)
Nonconventional Organics				
Acetone	5,079,688	154	13,339,234	1,607,106
Acetonitrile	926,804	0	574,641	0
n-Amyl acetate	333,871	0	639,973	824,830
Amyl alcohol	54,000	0	144,619	0

Table 9-1

(Continued)

Pollutant	A and C Direct Dischargers	B and D Direct Dischargers	A and C Indirect Dischargers	B and D Indirect Dischargers
Aniline	36,400	0	30,551	0
2-Butanone (MEK)	13,633	0	19,578	0
n-Butyl acetate	763,200	0	415,426	0
n-Butyl alcohol	392,049	0	978,684	109
tert-Butyl alcohol	86,997	0	212,508	0
Cyclohexane	339,512	0	22,082	0
Diethylamine	0	0	325,570	0
Diethyl ether	264,971	0	311,071	589
N,N-Dimethylacetamide	7,460	0	1,379,516	0
Dimethylamine	21,177	0	661,381	0
N,N-Dimethylaniline	0	0	131,174	0
N,N-Dimethylformamide	4,571,456	0	801,666	0
Dimethyl sulfoxide	87,992	0	819,972	355
1,4-Dioxane	0	0	69,039	0
Ethanol	4,149,197	67,674	8,847,220	2,525,138
Ethyl acetate	3,928,205	0	2,428,264	14,675
Ethylene glycol	45,399	0	326,623	18,061
Formaldehyde	701,800	230	783,013	2,418
Formamide	3,337	0	352,661	0
Furfural	18,056	0	30	0
n-Heptane	63,050	0	74,346	0
n-Hexane	1,838,778	0	1,566,893	14,624
Isobutyraldehyde	8,501	0	36,479	0
Isopropanol	5,396,359	38,672	9,095,624	853,366
Isopropyl acetate	527,801	0	249,114	225,593

Table 9-1

(Continued)

Pollutant	A and C Direct Dischargers	B and D Direct Dischargers	A and C Indirect Dischargers	B and D Indirect Dischargers
Isopropyl ether	878	0	16,730	350
Methanol	29,136,700	458	21,633,682	99,880
Methylamine	508,763	0	446,024	0
Methyl cellosolve	0	0	1,755,690	0
Methyl formate	607,950	0	28,689	0
2-Methylpyridine	98,800	0	0	0
Methyl isobutyl ketone (MIBK)	13,900	0	2,416,611	0
Petroleum naphtha	728	0	578,795	146
Polyethylene glycol 600	0	200	93,907	181
n-Propanol	1,101	0	19,326	0
Pyridine	617,929	0	321,010	1,803
Tetrahydrofuran	183,257	0	816,347	0
Trichlorofluoromethane	0	0	5,770	17,381
Triethylamine	600,080	0	1,693,165	2
Xylenes	724,196	0	153,563	0
Nonconventional Organics Subtotal	**62,153,975**	**107,388**	**74,616,261**	**6,206,607**
Ammonia (Aqueous)	2,443,575	28	4,620,458	302
Nonconventional Total	**64,597,550**	**107,416**	**79,236,719**	**6,206,909 (a)**

(a) Untreated load for facilities for which questionnaire data were available. Estimated total priority and nonconventional pollutant load for all facilities is 7,183,909 lbs/yr. See Section 9.2.

NA - Not available

Table 9-2

Current Pollutant Discharge Loads by Subcategory Group and Discharge Mode (lbs/yr)

Pollutant	A and C Direct Dischargers	B and D Direct Dischargers	A and C Indirect Dischargers	B and D Indirect Dischargers
Conventionals and COD				
BOD_5	3,258,176	57,455	NA	NA
COD	31,676,918	293,661	NA	NA
TSS	6,333,181	82,404	NA	NA
Priority Organics				
Benzene	0	0	120,200	0
Chlorobenzene	0	0	5,606	0
Chloroform	2,018	0	177,287	32
Chloromethane (Methyl chloride)	140,070	0	134	0
o-Dichlorobenzene (1,2-Dichlorobenzene)	0	0	21,499	0
1,2-Dichloroethane	103,934	0	4,294	0
Methylene chloride	145,518	0	1,198,531	15,595
Phenol	9,000	0	1,206	714
Toluene	122,269	0	257,685	5
Priority Organics Subtotal	**522,809**	**0**	**1,786,442**	**16,346**
Cyanide	45	0	1,084	0
Priority Pollutant Total	**522,854**	**0**	**1,787,526**	**16,346 (a)**
Nonconventional Organics				
Acetone	21,727	8	3,004,969	43,136
Acetonitrile	9,020	0	423,821	0
n-Amyl acetate	6,071	0	208,429	82,483
Amyl alcohol	53,000	0	143,554	0

Table 9-2

(Continued)

Pollutant	A and C Direct Dischargers	B and D Direct Dischargers	A and C Indirect Dischargers	B and D Indirect Dischargers
Aniline	0	0	4,600	0
2-Butanone (MEK)	908	0	17,283	0
n-Butyl acetate	97,500	0	415,426	0
n-Butyl alcohol	392,049	0	666,216	108
tert-Butyl alcohol	2,844	0	95,564	0
Cyclohexane	51	0	440	0
Diethylamine	0	0	218,020	0
Diethyl ether	307	0	454	589
N,N-Dimethylacetamide	746	0	1,045,358	0
Dimethylamine	756	0	660,593	0
N,N-Dimethylaniline	0	0	18,155	0
N,N-Dimethylformamide	174	0	387,124	0
Dimethyl sulfoxide	5,040	0	745,181	355
1,4-Dioxane	0	0	24,422	0
Ethanol	451,601	7,854	4,368,801	1,283,544
Ethyl acetate	51,583	0	205,545	3
Ethylene glycol	1,939	0	147,760	18,061
Formaldehyde	21,181	229	310,677	1,083
Formamide	109	0	7,075	0
Furfural	15,404	0	0	0
n-Heptane	50	0	27,894	0
n-Hexane	2,180	0	8,449	100
Isobutyraldehyde	0	0	35,654	0
Isopropanol	455,581	14,841	2,785,586	89,648
Isopropyl acetate	10,556	0	14,809	22,559

Table 9-2

(Continued)

Pollutant	A and C Direct Dischargers	B and D Direct Dischargers	A and C Indirect Dischargers	B and D Indirect Dischargers
Isopropyl ether	801	0	10,963	350
Methanol	1,905,851	98	12,433,615	44,747
Methylamine	23,400	0	310	0
Methyl cellosolve	0	0	445,137	0
Methyl formate	9,843	0	2,773	0
2-Methylpyridine	48,800	0	0	0
Methyl isobutyl ketone (MIBK)	11,000	0	623,193	0
Petroleum Naphtha	0	0	260,583	0
Polyethylene Glycol 600	0	200	87,039	181
n-Propanol	1,101	0	11,439	0
Pyridine	50	0	210,186	1,803
Tetrahydrofuran	90,808	0	226,167	0
Trichlorofluoromethane	0	0	3,850	0
Triethylamine	98,600	0	531,326	1
Xylenes	2,432	0	24,969	0
Nonconventional Organics Subtotal	**3,793,063**	**23,230**	**30,863,409**	**1,588,751**
Ammonia (Aqueous)	817,732	0	530,851	25
Nonconventional Total	**4,610,795**	**23,230**	**31,394,260**	**1,588,776 (a)**

(a) Load for facilities for which questionnaire data were available. Estimated total priority and nonconventional pollutant load for all facilities is 2,065,224 lbs/yr. See Section 9.3.

NA - Not available

Table 9-3

End-of Pipe Discharge Loads for Subcategory A and C Facilities Under BAT Options (lbs/yr)

Pollutant	BAT Option 1	BAT Option 2	BAT Option 3	BAT Option 4
Priority Organics				
Chloroform	250	250	250	250
Chloromethane (Methyl chloride)	1,155	1,111	1,111	1,111
1,2-Dichloroethane	250	59	40	40
Methylene chloride	2,705	304	304	304
Phenol	1	1	1	1
Toluene	261	261	261	261
Priority Organics Subtotal	**4,622**	**1,986**	**1,967**	**1,967**
Cyanide	7	7	7	7
Priority Pollutant Total	**4,629**	**1,993**	**1,974**	**1,974**
Nonconventional Organics				
Acetone	709	519	519	519
Acetonitrile	127	127	127	127
n-Amyl acetate	6,071	5,353	5,353	5,353
Amyl alcohol	720	360	360	360
2-Butanone (MEK)	825	825	824	824
n-Butyl acetate	10,521	10,521	10,521	10,521
n-Butyl alcohol	5,260	5,260	1,052	1,052
tert-Butyl alcohol	2,844	1,955	1,955	1,955
Cyclohexane	22	22	22	22
Diethyl ether	307	307	250	250
N,N-Dimethylacetamide	23	23	23	23
Dimethylamine	6	6	6	6
N,N-Dimethylformamide	39	39	39	39

Table 9-3

(Continued)

Pollutant	BAT Option 1	BAT Option 2	BAT Option 3	BAT Option 4
Dimethyl sulfoxide	121	121	121	121
Ethanol	22,299	17,407	11,571	11,571
Ethyl acetate	20,366	13,603	13,603	13,603
Ethylene glycol	1,939	1,939	1,939	1,939
Formaldehyde	8,056	8,056	8,056	8,056
Formamide	109	109	109	109
Furfural	15,404	14,123	10,525	10,525
n-Heptane	50	50	50	50
n-Hexane	47	47	47	47
Isopropanol	6,808	1,341	1,341	1,341
Isopropyl acetate	1,051	1,051	1,051	1,051
Isopropyl ether	801	801	800	800
Methanol	24,375	12,700	12,700	12,700
Methylamine	1,052	1,052	1,052	1,052
Methyl formate	2,211	1,685	1,685	1,685
2-Methylpyridine	105	105	105	105
Methyl isobutyl ketone (MIBK)	631	105	105	105
n-Propanol	1,101	1,101	1,052	1,052
Pyridine	1	1	1	1
Tetrahydrofuran	27,922	1,855	1,855	1,855
Triethylamine	1,052	1,052	1,052	1,052
Xylenes	100	100	100	100
Nonconventional Organics Subtotal	**163,076**	**103,721**	**89,971**	**89,971**
Ammonia	71,168	17,159	17,159	17,159
Nonconventional Pollutant Total	**234,244**	**120,880**	**107,130**	**107,130**

Values have not been rounded to significant figures.

Table 9-4

End-of-Pipe Discharge Loads for Subcategory B and D Facilities Under BAT Options (lbs/yr)

Pollutant	BAT Option 1	BAT Option 2	BAT Option 3	BAT Option 4
Acetone	8	8	8	8
Ethanol	189	145	94	94
Formaldehyde	63	63	63	63
Isopropanol	62	11	11	11
Methanol	98	92	92	92
Polyethylene Glycol 600	200	200	200	200
Nonconventional Pollutant Total (a)	**620**	**519**	**468**	**468**

(a) There are no priority pollutant end-of-pipe discharge loads for Subcategory B and D direct discharging facilities.

Values have not been rounded to significant figures.

Table 9-5

End-of-Pipe Discharge Loads for Subcategory A and C Facilities Under PSES Options (lbs/yr)

Pollutant	PSES Option 1	PSES Option 2	PSES Option 3	PSES Option 4
Priority Organics				
Benzene	252	252	25	25
Chlorobenzene	444	444	44	44
Chloroform	79	79	79	79
Chloromethane (Methyl chloride)	2	2	1	1
o-Dichlorobenzene (1,2-Dichlorobenzene)	8,330	1,083	3	3
1,2-Dichloroethane	3,443	700	26	26
Methylene chloride	1,541	1,541	160	160
Phenol	1,206	1,206	1,206	1,206
Toluene	2,136	2,136	188	188
Priority Organics Subtotal	**17,433**	**7,443**	**1,732**	**1,732**
Cyanide	62	62	62	62
Priority Pollutant Total	**17,495**	**7,505**	**1,794**	**1,794**
Nonconventional Organics				
Acetone	49,715	7,960	1,053	1,053
Acetonitrile	423,821	423,821	423,821	423,821
n-Amyl acetate	9,532	1,589	1,589	1,589
Amyl alcohol	41,742	1,245	473	473
Aniline	4,584	3,758	35	35
2-Butanone (MEK)	14,292	12,430	252	252
n-Butyl acetate	1,498	250	250	250
n-Butyl alcohol	487,817	8,284	396	396
tert-Butyl alcohol	95,564	7,785	2,744	2,744

Table 9-5

(Continued)

Pollutant	PSES Option 1	PSES Option 2	PSES Option 3	PSES Option 4
Cyclohexane	30	30	3	3
Diethylamine	6,355	958	42	42
Diethyl ether	422	244	63	63
N,N-Dimethylacetamide	1,045,358	1,045,358	26	26
Dimethylamine	4,835	90	3	3
N,N-Dimethylaniline	10,356	836	29	29
N,N-Dimethylformamide	387,124	387,124	195	195
Dimethyl sulfoxide	745,181	745,181	5,616	5,616
1,4-Dioxane	24,423	2,567	95	95
Ethanol	1,641,628	28,392	10,118	10,118
Ethyl acetate	14,496	3,291	3,291	3,291
Ethylene glycol	147,760	147,760	3,734	3,734
Formaldehyde	310,677	310,677	781	781
Formamide	4,249	2,274	916	916
n-Heptane	786	786	40	40
n-Hexane	373	373	30	30
Isobutyraldehyde	7,542	985	457	457
Isopropanol	569,547	31,294	1,181	1,181
Isopropyl acetate	8,350	2,041	2,041	2,041
Isopropyl ether	2,199	820	174	174
Methanol	9,810,898	34,527	12,491	12,491
Methylamine	310	310	34	34
Methyl cellosolve	2,537	2,537	2,537	2,537
Methyl formate	2,773	1,256	1,256	1,256
MIBK	5,106	1,950	25	25
Petroleum Naphtha	260,583	3,318	23	23

Table 9-5

(Continued)

Pollutant	PSES Option 1	PSES Option 2	PSES Option 3	PSES Option 4
Polyethylene Glycol 600	87,039	87,039	87,039	87,039
n-Propanol	11,439	757	28	28
Pyridine	6,695	6,695	82	82
Tetrahydrofuran	14,631	14,631	842	842
Trichlorofluoromethane	95	95	95	95
Triethylamine	11,899	2,235	403	403
Xylenes	194	194	30	30
Nonconventional Organics Subtotal	**16,274,455**	**3,333,747**	**564,333**	**564,333**
Ammonia	89,142	89,142	6,053	6,053
Nonconventional Pollutant Total	**16,363,597**	**3,422,889**	**570,386**	**570,386**

Values have not been rounded to significant figures.

Table 9-6

End-of-Pipe Discharge Loads for Subcategory B and D Facilities Under PSES Options (lbs/yr)

Pollutant	PSES Option 1	PSES Option 2	PSES Option 3
Priority Pollutants			
Methylene chloride	212	212	22
Phenol	714	714	714
Toluene	5	5	5
Priority Pollutant Total	**931**	**931**	**741**
Nonconventional Organics			
Acetone	4,281	557	557
n-Amyl acetate	4,233	705	705
n-Butyl alcohol	108	21	21
Diethyl ether	587	226	226
Dimethyl sulfoxide	355	355	355
Ethanol	462,587	4,212	4,212
Ethyl acetate	2	2	2
Ethylene glycol	18,061	18,061	18,061
Formaldehyde	1,083	1,083	1,083
n-Hexane	1	1	0
Isopropanol	16,825	809	809
Isopropyl acetate	4,233	705	705
Isopropyl ether	25	3	0
Methanol	37,231	927	927
Polyethylene Glycol 600	181	181	181
Pyridine	27	27	27
Triethylamine	1	1	1
Nonconventional Organics Subtotal	**549,821**	**27,876**	**27,872**
Ammonia	25	25	25
Nonconventional Pollutant Total	**549,846**	**27,901**	**27,897**

Values have not been rounded to significant figures.

Table 9-7

Pollutant Load Reduction Through Advanced Biological Treatment for Subcategory A and C and B and D Direct Dischargers (lbs/yr)

Pollutant	Load Reduction for A and C Direct Dischargers	Load Reduction for B and D Direct Dischargers
Priority Pollutants		
Benzene	0	0
Chlorobenzene	0	0
Chloroform	1,768	0
Chloromethane (Methyl chloride)	138,915	0
o-Dichlorobenzene (1,2-Dichlorobenzene)	0	0
1,2-Dichloroethane	103,684	0
Methylene chloride	142,813	0
Phenol	8,999	0
Toluene	122,008	0
Priority Pollutant Total	**518,186**	**0**
Nonconventional Organics		
Acetone	21,018	0
Acetonitrile	8,893	0
n-Amyl acetate	0	0
Amyl alcohol	52,280	0
Aniline	0	0
2-Butanone (MEK)	83	0
n-Butyl acetate	86,979	0
n-Butyl alcohol	386,789	0
tert-Butyl alcohol	0	0
Cyclohexane	29	0
Diethylamine	0	0

Table 9-7

(Continued)

Pollutant	Load Reduction for A and C Direct Dischargers	Load Reduction for B and D Direct Dischargers
Diethyl ether	0	0
N,N-Dimethylacetamide	723	0
Dimethylamine	750	0
N,N-Dimethylaniline	0	0
N,N-Dimethylformamide	135	0
Dimethyl sulfoxide	4,919	0
1,4-Dioxane	0	0
Ethanol	429,302	7,665
Ethyl acetate	31,217	0
Ethylene glycol	0	0
Formaldehyde	13,125	166
Formamide	0	0
Furfural	0	0
n-Heptane	0	0
n-Hexane	2,133	0
Isobutyraldehyde	0	0
Isopropanol	448,772	14,779
Isopropyl acetate	9,505	0
Isopropyl ether	0	0
Methanol	1,881,476	0
Methylamine	22,348	0
Methyl cellosolve	0	0
Methyl formate	7,632	0
2-Methylpyridine	48,695	0
Methyl isobutyl ketone (MIBK)	10,369	0
Petroleum Naphtha	0	0

Table 9-7

(Continued)

Pollutant	Load Reduction for A and C Direct Dischargers	Load Reduction for B and D Direct Dischargers
Polyethylene Glycol 600	0	0
n-Propanol	0	0
Pyridine	49	0
Tetrahydrofuran	62,886	0
Trichlorofluoromethane	0	0
Triethylamine	97,548	0
Xylenes	2,332	0
Nonconventional Organics Subtotal	**3,629,987**	**22,610**
Ammonia	746,564	0
Nonconventional Pollutant Total	**4,376,551**	**22,610**

Values have not been rounded to significant figures.

Table 9-8

Pollutant Load Reduction Through In-Plant Steam Stripping Followed by End-of-Pipe Advanced Biological Treatment for Subcategory A and C and B and D Direct Dischargers (lbs/yr)

Pollutant	Load Reduction for A and C Direct Dischargers	Load Reduction for B and D Direct Dischargers
Priority Pollutants		
Benzene	789	0
Chlorobenzene	0	0
Chloroform	105,178	0
Chloromethane (Methyl chloride)	140,838	0
o-Dichlorobenzene (1,2-Dichlorobenzene)	0	0
1,2-Dichloroethane	153,164	0
Methylene chloride	1,884,443	25
Phenol	8,999	1
Toluene	354,311	0
Priority Total	**2,647,722**	**26**
Nonconventional Organics		
Acetone	1,415,661	14
Acetonitrile	9,013	0
n-Amyl acetate	718	0
Amyl alcohol	53,640	0
Aniline	11	0
2-Butanone (MEK)	11,547	0
n-Butyl acetate	89,071	0
n-Butyl alcohol	386,789	0
tert-Butyl alcohol	23,889	0
Cyclohexane	283,920	0
Diethylamine	0	0
Diethyl ether	20,327	0
N,N-Dimethylacetamide	3,056	0
Dimethylamine	994	0
N,N-Dimethylaniline	0	0
N,N-Dimethylformamide	15,912	0
Dimethyl sulfoxide	7,481	0
1,4-Dioxane	0	0

Table 9-8

(Continued)

Pollutant	Load Reduction for A and C Direct Dischargers	Load Reduction for B and D Direct Dischargers
Ethanol	1,841,705	23,740
Ethyl acetate	931,650	0
Ethylene glycol	7	0
Formaldehyde	18,173	166
Formamide	138	0
Furfural	1,333	0
n-Heptane	187	0
n-Hexane	993,009	0
Isobutyraldehyde	0	0
Isopropanol	2,136,153	15,167
Isopropyl acetate	464,930	0
Isopropyl ether	16	0
Methanol	3,260,025	35
Methylamine	500,527	0
Methyl cellosolve	0	0
Methyl formate	606,265	0
2-Methylpyridine	49,798	0
Methyl isobutyl ketone (MIBK)	10,935	0
Petroleum Naphtha	524	0
Polyethylene Glycol 600	0	0
n-Propanol	0	0
Pyridine	2,257	0
Tetrahydrofuran	120,186	0
Trichlorofluoromethane	0	0
Triethylamine	108,619	0
Xylenes	696,956	0
Nonconventional Organics Subtotal	**14,064,222**	**39,122**
Ammonia	1,794,369	(a)
Nonconventional Pollutant Total	**15,858,591**	**39,150**

[a]Ammonia is not a pollutant of concern for Subcategory B and/or D direct discharges. There would be incidental ammonia removal of 28 pounds/yr through this treatment train.

Values have not been rounded to significant figures.

Table 9-9

Pollutant Load Reduction Through In-Plant Steam Stripping With Distillation Followed by End-of-Pipe Advanced Biological Treatment for Subcategory A and C and B and D Direct Dischargers (lbs/yr)

Pollutant	Load Reduction for A and C Direct Dischargers	Load Reduction for B and D Direct Dischargers
Priority Pollutants		
Benzene	789	0
Chlorobenzene	0	0
Chloroform	105,178	0
Chloromethane (Methyl chloride)	140,838	0
o-Dichlorobenzene (1,2-Dichlorobenzene)	0	0
1,2-Dichloroethane	153,183	0
Methylene chloride	1,884,443	25
Phenol	8,999	1
Toluene	354,311	0
Priority Total	**2,647,741**	**26**
Nonconventional Organics		
Acetone	1,415,661	14
Acetonitrile	9,013	0
n-Amyl acetate	718	0
Amyl alcohol	53,640	0
Aniline	11	0
2-Butanone (MEK)	11,547	0
n-Butyl acetate	89,071	0
n-Butyl alcohol	390,997	0
tert-Butyl alcohol	23,889	0
Cyclohexane	283,920	0

Table 9-9

(Continued)

Pollutant	Load Reduction for A and C Direct Dischargers	Load Reduction for B and D Direct Dischargers
Diethylamine	0	0
Diethyl ether	20,384	0
N,N-Dimethylacetamide	3,056	0
Dimethylamine	994	0
N,N-Dimethylaniline	0	0
N,N-Dimethylformamide	15,912	0
Dimethyl sulfoxide	7,481	0
1,4-Dioxane	0	0
Ethanol	1,847,541	23,791
Ethyl acetate	931,650	0
Ethylene glycol	7	0
Formaldehyde	18,173	166
Formamide	138	0
Furfural	4,931	0
n-Heptane	187	0
n-Hexane	993,009	0
Isobutyraldehyde	0	0
Isopropanol	2,136,153	15,167
Isopropyl acetate	464,930	0
Isopropyl ether	16	0
Methanol	3,260,025	35
Methylamine	500,527	0
Methyl cellosolve	0	0
Methyl formate	606,265	0
2-Methylpyridine	49,798	0
Methyl isobutyl ketone (MIBK)	10,935	0

Table 9-9

(Continued)

Pollutant	Load Reduction for A and C Direct Dischargers	Load Reduction for B and D Direct Dischargers
Petroleum Naphtha	524	0
Polyethylene Glycol 600	0	0
n-Propanol	49	0
Pyridine	2,257	0
Tetrahydrofuran	120,186	0
Trichlorofluoromethane	0	0
Triethylamine	108,619	0
Xylenes	696,956	0
Nonconventional Organics Subtotal	**14,079,170**	**39,173**
Ammonia	1,794,369	(a)
Nonconventional Pollutant Total	**15,873,539**	**39,201**

[a]Ammonia is not a pollutant of concern for Subcategory B and/or D direct discharges. There would be incidental ammonia removal of 28 pounds/yr through this treatment train.

Values have not been rounded to significant figures.

Table 9-10

Pollutant Load Reduction Through In-plant Steam Stripping for Subcategory A and C and B and D Indirect Dischargers (lbs/yr)

Pollutant	Load Reduction for A and C Indirect Dischargers	Load Reduction for B and D Indirect Dischargers
Priority Pollutants		
Benzene*	119,948	0
Chlorobenzene*	5,172	0
Chloroform*	283,593	74
Chloromethane* (Methyl chloride)	133	0
o-Dichlorobenzene (1,2-Dichlorobenzene)	13,169	0
1,2-Dichloroethane	896	0
Methylene chloride*	4,273,969	694,415
Phenol	0	0
Toluene*	2,446,728	0
Priority Pollutant Total	**7,143,608**	**694,489**
Nonconventional Organics		
Acetone	5,853,155	1,004,881
Acetonitrile	0	0
n-Amyl acetate	208,112	691,691
Amyl alcohol	101,893	0
Aniline	20,116	0
2-Butanone (MEK)	3,065	0
n-Butyl acetate	413,928	0
n-Butyl alcohol	339,432	1
tert-Butyl alcohol	0	0
Cyclohexane*	637	0
Diethylamine	230,036	0

Table 9-10

(Continued)

Pollutant	Load Reduction for A and C Indirect Dischargers	Load Reduction for B and D Indirect Dischargers
Diethyl ether	283,746	2
N,N-Dimethylacetamide	0	0
Dimethylamine	655,768	0
N,N-Dimethylaniline	7,823	0
N,N-Dimethylformamide	0	0
Dimethyl sulfoxide	0	0
1,4-Dioxane	21,603	0
Ethanol	4,575,401	1,310,308
Ethyl acetate	1,496,135	3,864
Ethylene glycol	0	0
Formaldehyde	0	0
Formamide	108,285	0
Furfural	0	0
n-Heptane*	48,740	0
n-Hexane*	1,193,015	99
Isobutyraldehyde	28,755	0
Isopropanol	3,558,832	218,887
Isopropyl acetate	171,094	199,482
Isopropyl ether	9,014	325
Methanol	5,657,638	8,271
Methylamine	12,871	0
Methyl cellosolve*	1,499,045	0
Methyl formate	5	0
2-Methylpyridine	0	0
Methyl isobutyl ketone (MIBK)	1,487,907	0
Petroleum Naphtha	0	0

Table 9-10

(Continued)

Pollutant	Load Reduction for A and C Indirect Dischargers	Load Reduction for B and D Indirect Dischargers
Polyethylene Glycol 600	0	0
n-Propanol	4,310	0
Pyridine	288,418	1,775
Tetrahydrofuran	450,622	0
Trichlorofluoromethane*	5,675	1
Triethylamine	940,711	1
Xylenes*	27,073	0
Nonconventional Organics Subtotal	**29,702,860**	**3,439,588**
Ammonia*	1,182,199	0
Nonconventional Pollutant Total	**30,885,059**	**3,439,588**

(a)Only a subset of the pollutants that would be treated by this technology would actually receive a standard under co-proposal (2). Those pollutants are marked with an asterisk.

Values have not been rounded to significant figures.

Table 9-11

Pollutant Load Reduction Through In-plant Steam Stripping With Distillation for Subcategory A and C and B and D Indirect Dischargers (lbs/yr)

Pollutant	Load Reduction for A and C Indirect Dischargers	Load Reduction for B and D Indirect Dischargers
Priority Pollutants		
Benzene*	119,948	0
Chlorobenzene*	5,172	0
Chloroform*	283,593	74
Chloromethane* (Methyl chloride)	133	0
o-Dichlorobenzene (1,2-Dichlorobenzene)	20,416	0
1,2-Dichloroethane	3,639	0
Methylene chloride*	4,273,969	694,415
Phenol	0	0
Toluene*	2,446,728	0
Priority Pollutant Total	**7,153,598**	**694,489**
Nonconventional Organics		
Acetone	5,894,908	1,008,605
Acetonitrile	0	0
n-Amyl acetate	216,055	695,218
Amyl alcohol	142,391	0
Aniline	20,942	0
2-Butanone (MEK)	4,927	0
n-Butyl acetate	415,176	0
n-Butyl alcohol	818,966	88
tert-Butyl alcohol	87,779	0
Cyclohexane*	637	0

Table 9-11

(Continued)

Pollutant	Load Reduction for A and C Indirect Dischargers	Load Reduction for B and D Indirect Dischargers
Diethylamine	235,434	0
Diethyl ether	283,924	363
N,N-Dimethylacetamide	0	0
Dimethylamine	660,513	0
N,N-Dimethylaniline	17,343	0
N,N-Dimethylformamide	0	0
Dimethyl sulfoxide	0	0
1,4-Dioxane	43,458	0
Ethanol	6,188,635	1,768,683
Ethyl acetate	1,507,340	3,864
Ethylene glycol	0	0
Formaldehyde	0	0
Formamide	110,260	0
Furfural	0	0
n-Heptane*	48,740	0
n-Hexane*	1,193,015	99
Isobutyraldehyde	35,312	0
Isopropanol	4,097,086	234,901
Isopropyl acetate	177,402	203,009
Isopropyl ether	10,394	347
Methanol	15,434,007	44,576
Methylamine	12,871	0
Methyl cellosolve*	1,500,905	0
Methyl formate	1,522	0
2-Methylpyridine	0	0
Methyl isobutyl ketone (MIBK)	1,491,063	0

Table 9-11

(Continued)

Pollutant	Load Reduction for A and C Indirect Dischargers	Load Reduction for B and D Indirect Dischargers
Petroleum Naphtha	257,265	0
Polyethylene Glycol 600	0	0
n-Propanol	14,992	0
Pyridine	288,418	1,775
Tetrahydrofuran	450,622	0
Trichlorofluoromethane*	5,675	1
Triethylamine	950,375	1
Xylenes*	27,073	0
Nonconventional Organics Subtotal	**42,645,425**	**3,961,530**
Ammonia*	1,182,199	0
Nonconventional Pollutant Total	**43,827,624**	**3,961,530**

(*)Only a subset of the pollutants that would be treated by this technology would actually receive a standard under co-proposal (2). Those pollutants are marked with an asterisk.

Values have not been rounded to significant figures.

Table 9-12

Pollutant Load Reduction Through In-Plant Steam Stripping With Distillation Followed by End-of-Pipe Advanced Biological Treatment for Subcategory A and C Indirect Dischargers (lbs/yr)

Pollutant	Load Reduction for A and C Indirect Dischargers
Priority Pollutants	
Benzene*	120,175
Chlorobenzene*	5,572
Chloroform*	283,593
Chloromethane (Methyl chloride)*	134
o-Dichlorobenzene (1,2-Dichlorobenzene)	21,496
1,2-Dichloroethane	4,313
Methylene chloride*	4,275,350
Phenol	0
Toluene*	2,448,677
Priority Pollutant Total	**7,159,310**
Nonconventional Organics	
Acetone	5,901,816
Acetonitrile	0
n-Amyl acetate	216,055
Amyl alcohol	143,163
Aniline	24,666
2-Butanone (MEK)	17,105
n-Butyl acetate	415,176
n-Butyl alcohol	826,854
tert-Butyl alcohol	92,820
Cyclohexane*	664
Diethylamine	236,350

Table 9-12

(Continued)

Pollutant	Load Reduction for A and C Indirect Dischargers
Diethyl ether	284,104
N,N-Dimethylacetamide	1,045,332
Dimethylamine	660,600
N,N-Dimethylaniline	18,150
N,N-Dimethylformamide	386,929
Dimethyl sulfoxide	739,565
1,4-Dioxane	45,930
Ethanol	6,206,910
Ethyl acetate	1,507,340
Ethylene glycol	144,027
Formaldehyde	309,897
Formamide	111,618
Furfural	0
n-Heptane*	49,486
n-Hexane*	1,193,356
Isobutyraldehyde	35,840
Isopropanol	4,127,199
Isopropyl acetate	177,402
Isopropyl ether	11,039
Methanol	15,456,041
Methylamine	13,147
Methyl cellosolve*	1,499,045
Methyl formate	1,522
2-Methylpyridine	0
Methyl isobutyl ketone (MIBK)	1,492,987
Petroleum Naphtha	260,560

Table 9-12

(Continued)

Pollutant	Load Reduction for A and C Indirect Dischargers
Polyethylene glycol 600	0
n-Propanol	15,720
Pyridine	295,031
Tetrahydrofuran	464,412
Trichlorofluoromethane*	5,675
Triethylamine	952,206
Xylenes*	27,237
Nonconventional Organics Subtotal	**45,412,976**
Ammonia*	1,265,289
Nonconventional Pollutant Total	**46,678,265**

(*)Only a subset of the pollutants that would be treated by this technology would actually receive a standard under co-proposal (2). Those pollutants are marked with an asterisk.

Values have not been rounded to significant figures.

REFERENCES

1. Memorandum: Subcategory D Indirect Scale-up Methodology, from K. Mahsman, Radian Corporation, to the Public Record, September 1994.

2. Memorandum: Final Pollutant Loading Estimates for the Pharmaceutical Manufacturing Industry - Subcategory A/C and B/D Direct and Indirect Discharging Facilities, from K. Mahsman and M. Willett, Radian Corporation, to F. Hund, USEPA/EAD, August 31, 1994.

3. Letter from M. Willett, Radian Corporation, to K. Koon, Versar, December 15, 1994.

SECTION 10

COSTS OF TECHNOLOGY BASES FOR REGULATIONS

10.1 Introduction

Previous sections have described the respective BPT, BCT, BAT, NSPS, PSES, and PSNS technology options that were considered as the bases of regulations for the pharmaceutical manufacturing industry. This section presents the estimated engineering costs associated with installing and operating each of these technology bases. These costs are calculated to determine the overall economic impact on the industry of complying with each regulatory option.

The following information is discussed in this section:

- Section 10.2 discusses the costing methodology;
- Section 10.3 discusses cost modeling and summarizes cost estimating assumptions and design bases for the technologies that make up the regulatory options; and
- Section 10.4 presents the cost estimates by regulatory option.

10.2 Costing Methodology

To accurately determine the impact of the proposed effluent limitations guidelines and standards on the pharmaceutical manufacturing industry, it is necessary to calculate costs associated with regulatory compliance. A cost model was developed to represent each of the regulatory options under BPT, BCT, BAT, PSES, PSNS, and NSPS. The cost model is used to calculate costs for each option based on the treatment technologies used as the basis for that option. These costs are estimates of actual compliance costs; however, the

regulations do not require that a facility install or possess the technologies specified as the bases, but only that the appropriate limitations be met.

The Agency has selected a facility-by-facility approach to costing as opposed to a model facility approach, because of the variability of processes and resultant wastewaters among pharmaceutical manufacturing facilities. Detailed facility information was available from responses to the Detailed Questionnaire, which was used to characterize the wastewater and assess existing treatment technologies at each facility. It should be noted, however, that in certain instances, engineering assumptions regarding facility operations were made, or industry average data were used when facility-specific information were not available. Thus, for any given facility, the costs estimated may deviate from those that would actually be experienced by the facility. However, since these assumptions were based on industry-wide data, the resulting estimates are considered accurate when evaluated on an industry-wide, aggregate basis.

When practical and appropriate, facilities were given credit for existing treatment on site, based on an evaluation of the following criteria:

- Biological treatment system aeration capacity (in million gallons);
- Clarifier overflow rate (in gallons per minute per square foot);
- Presence of adequate equalization treatment;
- Presence of steam stripping or steam stripping with distillation treatment that achieved adequate removal of organic compounds; and
- Presence of cyanide destruction treatment - this credit was given wholly or partially based on comparison to the treatment system selected as the technology basis.

These treatment credits were used to develop cost estimates for system upgrades instead of new systems where appropriate. At facilities that currently meet the proposed

limitations associated with a regulatory option, no compliance costs beyond necessary additional monitoring were estimated.

10.2.1 Cost Model Structure

The model used to calculate wastewater treatment costs was developed based on research into various existing costing approaches and use of customized computer software tools. The model consists mainly of a series of technology modules, each of which calculates the costs associated with a particular treatment technology. These modules can be combined as appropriate to assemble each of the various regulatory options. A more detailed discussion of the cost model and its origins is given in Section 10.3.

Operation and maintenance (O&M) and capital costs were calculated by the model for each technology and then summed for all technologies at each facility. The facility capital and O&M costs were combined and totaled by subcategory and discharge type (e.g. Subcategory A and C - indirect discharger).

Annual O&M costs consist of all costs related to operating and maintaining the treatment system for a period of one year. Sources for O&M costs primarily included literature references and engineering judgement (typically used in the case of estimating required operator hours). O&M costs typically include the following:

- Chemical usage;
- O&M labor;
- Removal, transportation, and disposal of any waste solids, sludges, solvents, or other waste products generated by the treatment system;
- Any required treatment unit performance monitoring not related to actual compliance monitoring (e.g., breakthrough monitoring between beds of the GAC system); and

- Utilities, such as electricity and steam, required to run the treatment system.

Table 10-1 presents the O&M unit costs most commonly used by the model and includes references for the origin of each cost.

Capital costs consist of direct and indirect costs associated with purchase and installation of wastewater treatment equipment. Primary sources for the capital costs were vendor quotes and literature references. Table 10-2 presents the unit capital costs most commonly used by the model and includes references for the origin of each cost. Typically, direct capital costs include the following:

- Purchase and installation of treatment equipment;
- Purchase and installation of piping, instrumentation, pumps, and other ancillary equipment;
- Electrical hookups;
- Any required site preparation (e.g., excavation);
- Construction of buildings or other structures; and
- Land purchase.

In addition to direct capital costs, indirect costs are also included in the estimate of total capital cost. Indirect capital costs typically include engineering costs and contractor's fees.

For each technology, it is assumed that ancillary direct capital costs and required indirect capital costs can be accounted for by using a factor related to purchased and installed capital cost. Table 10-3 lists these factors for all applicable treatment technologies.

Because all facility-specific information in the questionnaire database is from 1990, all costs are adjusted to 1990 dollars. This adjustment allows direct comparison between reported financial data and costs for each facility. Costs are adjusted using the Marshall and Swift 1990 annual index (915.1) and the index value for the year in which the costs were originally reported using the following formula:

$$AC = OC(915.1/OCI) \qquad (10\text{-}1)$$

where: AC = Adjusted cost, $
OC = Original cost, $
OCI = Original cost year index

The wage rate for all required labor to properly operate and maintain the systems associated with the technology bases was obtained from the U.S National Bureau of Labor Statistics. In 1990, the average wage rate for all production workers in the Drugs Manufacturing industry was $12.90 per hour. This rate was then increased by 115% to account for supervision (15%), and overhead (100%) to arrive at a total rate of $27.74 per hour. The cost for electricity used by various treatment technologies was obtained from 1990 U.S Department of Energy statistics for Investor-Owned Utilities for Commercial Facilities. This rate was given as $0.048 per kilowatt-hour. The cost for steam usage was assumed to be $3.20 per 1,000 pounds of 100 psig steam. This value was taken from Plant Design and Economics for Chemical Engineers, Peters and Timmerhaus, Fourth Edition, and represents the high end of the range of costs given for 100 psig steam. These unit costs are listed along with other O&M unit costs in Table 10-1.

For the cost estimating effort, it was assumed that all Subcategory A and C facilities and Subcategory B and D direct discharger facilities operate 350 days per year, and that Subcategory B and D indirect discharger facilities operate 250 days per year. These assumptions are based on operating modes observed during engineering site visits. It is

also assumed, because of the nature of the technology, that all biological treatment systems operate 365 days per year, regardless of subcategory.

10.3 Cost Modeling

10.3.1 Evaluation of Existing Cost Models

Before a costing methodology could be developed, existing cost models were researched and evaluated to determine which, if any, existing algorithms for costing various treatment technologies could be used to develop costs for wastewater treatment systems and treatment system upgrades in the pharmaceutical manufacturing industry. The following models were initially considered for potential use:

- The Wastewater Treatment System Design and Cost Model (WTSDCM) developed by EPA in the early 1980s for various metal manufacturing-related industries;
- The Cost of Remedial Action model (CORA);
- The Remedial Action Cost Engineering and Requirements (RACER) model;
- The Advanced System for Process Engineering (ASPEN);
- The Computer Assisted Procedure for the Design and Evaluation of wastewater Treatment systems (CAPDET); and
- The pesticide industry models developed by EPA for pesticide chemicals manufacturers and pesticide formulators, packagers, and repackagers, respectively.

The WTSDCM model was eliminated because of the lack of similarity between pharmaceutical and metal manufacturing industry wastewaters and related treatment techniques. The CORA model was also eliminated because it had been superseded by

the more recently developed RACER model. The remainder of the cost models were considered further.

The RACER model was determined not to be applicable because it was designed to address remedial treatment activities associated with cleanup of contaminated sites, and not industrial wastewater treatment. ASPEN was also determined not to be applicable because, while serving as an excellent process simulation tool, it is not set up to serve the cost estimating purposes required. It also models only the steam stripping and distillation treatment technologies included in the basis for the regulatory options.

The remaining models (CAPDET and the pesticide industry models) were determined to have some appropriate design and costing information, but were not configured properly to be used directly to cost the pharmaceutical manufacturing industry. Based on this conclusion, it was determined that the most effective way to model costs for the industry would be through development of a new cost model.

The resulting cost model is an integrated computer model that uses design and costing information taken from many sources, including CAPDET and the pesticides industry models. The cost model includes program files that design and cost all technologies included as bases for the regulatory options discussed in Section 7.2, and data files that include all pertinent facility data.

10.3.2 Model Driver

Because the pharmaceutical manufacturing industry cost model (hereafter referred to as the cost model) is basically a collection of computer "modules" designed to calculate costs for each of the basic technologies, it was necessary to include a program to organize the modules and track the costs for the entire industry. This program has been designated as the model "driver". The model driver performs the following major functions associated with generating industry costs for each of the regulatory options:

- Locate and open all necessary input data files;
- Store input data entered by a user of the model;
- Open and run each of the technology modules in the appropriate order;
- Track all costs and pollutant concentrations generated by the technology modules; and
- Send tracked costs by subcategory, discharge type, and regulatory option to a storage file which may be printed or maintained in electronic form.

The following sections list the major technologies included as modules within the cost model, and describe the major assumptions and costing methodology used for each.

10.3.3 Advanced Biological Treatment

Advanced biological treatment is used to control BOD_5, COD, and TSS and to degrade various organic pollutants. Biological treatment systems are normally designed based on BOD_5 and TSS loads and desired removal efficiency. Organic pollutant reduction also occurs through well-operated treatment systems. The installation of extended aeration activated sludge biological treatment was assumed for cost estimating purposes. As shown in Table 7-1, activated sludge treatment is the most common biological treatment used in the pharmaceutical manufacturing industry. All of the facilities that form the bases for the limitations based on biological treatment use activated sludge biological treatment on site.

Typically, an extended aeration activated sludge biological treatment system consists of the following major equipment:

- An equalization basin;
- An aeration basin;
- A secondary clarifier; and
- A sludge handling system, if necessary.

10.3.3.1 Overview of Costing Methodology

Facilities requiring additional treatment of BOD_5, COD, TSS, or ammonia (if applicable) were costed for installing a biological treatment system capable of removing these pollutants down to the long-term mean performance concentrations for this technology that are discussed in Section 8.5. If a facility had no biological treatment on site, a new treatment system was costed. If a facility had biological treatment on site, an upgrade to the existing system was costed.

Various types of upgrades were possible for a facility with existing treatment on site. If additional BOD_5 or COD removal was required, an additional aeration basin was installed in parallel with the existing treatment unit. If additional TSS treatment was also required, additional clarifiers were installed in parallel with the existing clarifiers.

If a facility required additional TSS treatment only, polymer was added to the existing clarifiers to enhance settling. If only additional ammonia treatment was required, surface aerators were added to the existing aeration basin to enhance the growth of nitrifying microorganisms.

If the costed biological treatment system, whether an upgrade or new system, was determined to generate excess biological solids, a new sludge handling system was installed. The following table shows the breakdown between facilities requiring upgrades and facilities requiring completely new biological treatment systems.

Subcategory	Discharge type	Based on BPT Option 2			Total	Based on PSES Option 3			Total
		Upgrades	New Systems	Already in compliance		Upgrades	New Systems	Already in compliance	
A and C	Direct	9	5	10	24	NA	NA	NA	
A and C	Indirect	NA	NA	NA		63	5	20	88
B and D	Direct	3	2	9	14	NA	NA	NA	
B and D	Indirect	NA	NA	NA		NA	NA	NA	111

10.3.3.2 Design Bases and Assumptions

The design of the aeration basin and secondary clarifier are based on a combination of relationships and equations developed by Eckenfelder and from field data for suspended growth biological treatment. Costing equations were taken from CAPDET for equalization basins, package extended aeration activated sludge units (facility flows less than 0.5 MGD), full-size extended aeration activated sludge units (flows greater than 0.5 MGD), and circular secondary clarifiers.

Design equations for biological treatment systems were similar for new units and for upgrades. The following is a list of key design assumptions for costing biological treatment for pharmaceutical manufacturing facilities:

- Values for key design parameters associated with biological treatment were established based on subcategory-specific information obtained from the Detailed Questionnaire. These values are listed in Table 10-4.
- The retention time for designed clarifiers is 5 hours.
- The retention time for designed equalization basins is 24 hours (if a new equalization basin is necessary).
- The sludge generated by the biological treatment unit has the following characteristics:
  - 1% solids in the sludge from the clarifier to the sludge thickener;
  - 5% solids in the sludge from the thickener to the filter press;
  - 13% solids in filter press cake; and
  - Sludge density equal to 80 lbs/ft^3.
- Generated sludge is thickened, dewatered, and hauled off site for incineration as a nonhazardous waste.

- Installation of any of the equipment associated with biological treatment will not require purchase of additional land.

- One or more floating surface mixers are necessary for operation of the equalization basin. (It is assumed that 30 horsepower per million gallons are required for mixing in the equalization basin.)

- Floating surface aerators will be used for ammonia treatment upgrades, and fix-mounted surface aerators will be used for treatment of BOD_5 and COD.

10.3.3.3 Costing Methodology

Cost equations for purchase and installation of equipment associated with equalization, aeration, and secondary clarification were obtained from CAPDET. The costs for the following standard-sized equipment were also obtained from CAPDET: package aeration plant (100,000 gal/day) and clarification tank (90-foot diameter). The following costs were obtained from vendors or costing references: chemical unit costs, excavation unit cost, reinforced concrete installation unit cost, floating surface aerator costs, fixed-mounted surface aerator costs, sludge thickening tank costs, sludge filter press costs, and sludge hauling and disposal costs. Tables 10-1 and 10-2 presents all unit costs listed above.

The following are included in the total capital cost calculated for each facility requiring biological treatment (all equipment costs include purchase and installation):

- A reinforced, concrete equalization basin (if not already existing at the facility);

- Floating surface mixers for the equalization basin, if necessary;

- Floating surface aerators in an existing aeration basin for the nitrification of ammonia, if necessary;

- A reinforced concrete aeration basin, with associated fixed-mounted surface aerators, if necessary (aeration basins are provided at

facilities with no existing biological treatment, or where existing treatment is not adequate);

- A reinforced concrete clarifier, if necessary (clarifiers are provided at facilities with no existing biological treatment, or where existing suspended solids removal is not adequate);
- Any earthwork required for site preparation prior to installing the equalization basin, aeration basin, or clarifier (earthwork includes the construction of curbs and dikes for secondary containment);
- A platform and pedestrian bridge over the aeration basin;
- Sludge thickening tank(s); and
- Filter press(es) for sludge dewatering.

Table 10-3 presents the factors that are used by the cost model to account for ancillary direct and all indirect capital costs.

The following are included in the total O&M costs calculated for each facility:

- O&M labor;
- Electricity usage;
- Chemical purchases;
- Miscellaneous O&M materials and supplies; and
- Sludge hauling and incineration.

Table 10-5 lists operation and maintenance labor hour requirements for various activities associated with biological treatment.

All operation and maintenance hour requirement calculations except those used for sludge handling were based on assumptions and equations from CAPDET. Sludge handling labor hour requirements were developed based on engineering judgement regarding the labor required for operation and maintenance of the filter press or presses.

Electricity usage was calculated using relationships provided in CAPDET. Electricity requirement equations for each portion of the biological treatment system are shown below.

Activity	Electricity Usage Equation (a)
Package aeration	75,000 (FLOW)
Full-scale aeration	6701.4 (TICA) (b)
Clarification	7500 (SA ≤ 1670) 2183.3 $(SA)^{0.1663}$ (1670 < SA ≤ 16,700) 38.4 $(SA)^{0.5818}$ (SA > 16,700)
Sludge Handling	None

(a) All equations yield values in kilowatt-hours.
(b) This equation represents operating aerators 90% of the time, every day, year-round.
FLOW - Facility flowrate (MGD).
TICA - Total installed capacity of aeration (horsepower).
SA - Clarifier surface area (ft^2).

Miscellaneous O&M material and supply costs are based on factors provided in CAPDET. These factors are listed for biological treatment operations below.

Activity	Miscellaneous O&M Cost
Package aeration	1.74 $(FLOW)^{-0.2497}$
Full-size aeration	4.225 - 0.975log (TICA)
Clarification	1 percent of total clarification purchased and installed equipment costs

FLOW - Facility flowrate (MGD)
TICA - Total installed capacity of aeration (horsepower)

Table 10-1 lists unit costs for chemical purchases and sludge hauling and incineration.

10.3.4 Multimedia Filtration

Multimedia filtration is a treatment technology used primarily for the removal of TSS from wastewater. This technology can be used as an end-of-pipe treatment to remove

biological or other suspended solids prior to off-site discharge, or as a pretreatment technology prior to activated carbon treatment or other technologies that may be adversely affected by high TSS concentrations. Multimedia filtration is considered to be superior to sand or other single-media filtration technologies due to increased flow capacity and higher efficiency.

Multimedia filtration was costed for all options that included filtration at facilities where current TSS concentrations exceeded the long-term mean concentration for filtration.

The physical equipment required for this treatment includes a filtration unit with multiple filter cells (to allow continuous operation during maintenance of individual cells), a backwash tank and pump, and all internal piping and electrical controls associated with operating the treatment unit. For filters with a surface area greater than 400 square feet, the filtration unit and backwash tank are both assumed to be constructed of reinforced concrete. Package filtration units are installed for facilities requiring a filter surface area of 400 ft^2 or less. Materials of construction vary for package filtration units.

10.3.4.1 Overview of Costing Methodology

Cost estimates for multimedia filtration units were developed for those facilities with reported TSS concentrations in the final effluent above the long-term mean concentrations. No credit was given to facilities for filtration units existing on site unless they currently achieve the long-term mean performance level associated with filtration.

There were situations where facilities did incur costs for TSS treatment even if they achieved the long-term mean performance level. This occurred when facilities required biological treatment as part of a technology option that also included filtration. It was assumed that the biological system discharged wastewater containing TSS at the long-term mean concentration associated with biological treatment. This concentration may

have been higher than the TSS concentration reported in the Detailed Questionnaire for a particular facility.

10.3.4.2 Design Bases and Assumptions

Design equations for multimedia filtration were taken directly from CAPDET. The following is a list of key design assumptions associated with costing multimedia filtration treatment.

- Facilities would not be required to purchase additional land to install this technology;
- Package filtration units are installed for facilities requiring a filter surface area of 400 ft^2 or less;
- For units requiring greater than 400 ft^2 of filter surface area, a standard unit size of 784 ft^2 is used as a basis for purchase cost equations;
- Backwashing is performed, when necessary, at a rate of 20 gpm/ft^2 for 10 minutes at a time;
- The system is assumed to be gravity flow; and
- The hydraulic loading rates used to size the new units are based on industry averages (3.37 gpm/ft^2 for Subcategory A and C facilities and 2.23 gpm/ft^2 for Subcategory B and D facilities).

Table 10-3 presents the factors used by the model to account for ancillary direct and all indirect costs.

10.3.4.3 Costing Methodology

Costing equations and values were taken from CAPDET and vendor information. The following unit costs were obtained from CAPDET: package filtration and full-size

filtration standard unit costs. Unit costs for earthwork and reinforced concrete wall installation are based on vendor information. Tables 10-1 and 10-2 present all of these unit costs.

The following are included in the total capital cost calculated for each facility requiring multimedia filtration treatment:

For Package Filtration	For Full-Scale Filtration
• Earthwork associated with installation of backwash tank (earthwork includes the construction of curbs and dikes for secondary containment);	• Earthwork associated with installation of the filter unit and backwash tank (earthwork includes the construction of curbs and dikes for secondary containment);
• Construction of the concrete backwash tank;	• Construction of the concrete filter unit and concrete backwash tank;
• Purchase of package filter unit; and	• Purchase of required filtration equipment; and
• Installation of equipment (assumed by CAPDET to be 53% of the concrete installation cost).	• Installation of equipment (assumed by CAPDET to be 53% if the concrete installation cost).

Factors to account for ancillary direct and all indirect capital costs were taken from CAPDET, and are listed in Table 10-3.

As mentioned earlier, filters larger than 400 ft^2 were costed using 784 ft^2 as a standard size. The equations for calculating the cost of these filters are:

$$\text{If SAD} \leq 784 \text{ ft}^2$$

$$\text{COST} = [1.04\ (\text{SAD})^{0.6853}]\ \frac{(\text{STANDARD})}{100} \qquad (10\text{-}2)$$

$$\text{If SAD} > 784 \text{ ft}^2$$

$$COST = [8.99\ (SAD)^{0.3615}]\ \frac{(STANDARD)}{100} \qquad (10\text{-}3)$$

where:
COST = The capital cost of the filter unit, $
SAD = The designed filter surface area, ft^2
STANDARD = The capital cost of a 784 ft^2 filtration unit, $.

The following are included as O&M costs for multimedia filtration treatment:

- O&M labor;
- Miscellaneous O&M materials (assumed by CAPDET to be equal to 5% of the purchase cost of the filter unit); and
- Electricity usage.

Operation and maintenance labor requirements and electricity usage requirements are based on relationships provided in CAPDET. They are as follows:

- Operation labor (hrs) = $80.4\ (FLOW)^{0.572}$
- Maintenance labor (hrs) = $54\ (FLOW)^{0.585}$
- Electricity Usage (Kwh) = $8213(FLOW)^{0.972}$

where: FLOW = Facility flowrate (MGD).

10.3.5 Polishing Pond Treatment

Polishing pond treatment is used primarily to control TSS in wastewater. BOD_5 removal associated with the settling of suspended solids may also result from this treatment. This technology is most commonly used as a final end-of-pipe treatment prior to off-site discharge of wastewater.

Costs for polishing ponds were included for all options with polishing pond treatment as part of the technology basis at facilities where current long-term mean TSS concentrations exceed the long-term mean for polishing ponds.

The physical equipment required to perform polishing pond treatment includes influent and effluent structures (both assumed to be reinforced concrete), a pond or surface impoundment with an engineered, synthetic double liner system, and a groundwater detection monitoring system. It is assumed for cost estimating purposes that the installation of polishing ponds would require facilities to comply with all applicable RCRA regulations for surface impoundments used to manage hazardous waste. Typically, industrial wastewater treatment systems are excluded from complying with RCRA regulations. However, since a polishing pond meets the RCRA definition of a surface impoundment, and pharmaceutical wastewater typically contains listed hazardous wastes, RCRA hazardous waste regulations are assumed to apply to polishing ponds.

10.3.5.1 Overview of Costing Methodology

Costs for new polishing ponds were included for all facilities with reported TSS concentrations above long-term mean concentrations in end-of-pipe wastewater streams.

Cost estimates for all facilities requiring polishing pond treatment included a groundwater detection monitoring system and a RCRA closure plan. If the facility did not already have a RCRA Part B Permit (required for operators of surface impoundments that receive hazardous waste), costs were included for obtaining the permit.

10.3.5.2 Design Bases and Assumptions

The system designed and costed by the cost model is based primarily on equations developed for CAPDET. Important assumptions associated with this design include the following.

- The hydraulic detention time of the pond is 3 days.
- The depth of the pond is 5 feet.
- The excavation cut and fill volumes are approximately equalized to minimize the volume of fill required or soil removed from the construction site.
- Facilities would be able to purchase land contiguous to their existing facilities to install this treatment. Each facility was assigned a classification of "urban" or "rural", and purchased land was priced accordingly.
- Sludge settled in the bottom of the pond is removed once per year, hauled off site and disposed of by incineration.
- Monitoring wells installed as part of the groundwater detection monitoring system would be installed at 200-feet intervals around the perimeter of the pond, with a minimum of four wells installed.

10.3.5.3 Costing Methodology

All design and costing equations for polishing pond treatment were taken from CAPDET. Unit costs for the following were obtained from vendors: earthwork, reinforced concrete installation, double liner, monitoring well installation, annual and semiannual groundwater sampling and analysis, sludge removal, sludge hauling, sludge disposal, groundwater background concentration determination, groundwater monitoring plan development, RCRA closure plan development, and RCRA Part B permit development. Groundwater sampling and analysis costs were calculated based on compliance with RCRA regulations. Specific costing algorithms can be found in The

Pharmaceuticals Manufacturing Cost Documentation Report [1]. All other unit costs are presented in Tables 10-1 and 10-2. Land costs were estimated for urban and rural areas, respectively. A purchase cost of $10,000 per acre was assumed for urban facilities, and $2,000 per acre was assumed for rural facilities.

Costs for periodic sampling and analysis were scaled depending on the size of the pond. For pond sizes of one acre or smaller, the base costs listed below were used. For larger pond sizes, the base costs were multiplied by the number of acres (assuming the next largest whole number of acres).

Activity/Item	Cost (1990 $)	Unit/Standard Size
- Background Groundwater Sampling	114,868	per pond
- Semi-annual Groundwater Monitoring	57,434	per pond
- Annual Groundwater Monitoring	5,210	per pond

The following are included in the total capital cost calculated for each facility requiring polishing pond treatment:

- Purchase of land;
- Earthwork to prepare the area for pond construction;
- Construction of influent and effluent structures (reinforced concrete);
- An impermeable double liner system (this system consists of a synthetic liner underlain by 6 inches of sand containing the leachate collection system, underlain by another synthetic liner and another 6 inches of sand);
- A groundwater detection monitoring system;

- A RCRA closure plan; and
- A RCRA Part B permit application, if necessary.

Table 10-3 presents the factors used by the model to account for ancillary direct and all indirect capital costs.

The following are included in the total O&M costs calculated for each facility:

- O&M labor;
- Yearly groundwater sampling and analysis; and
- Sludge removal hauling and disposal.

Operation and maintenance labor requirements were calculated using assumptions and equations provided in CAPDET. It was assumed, for flow rates smaller than 0.1 MGD, that the total O&M labor requirement would be 160 hours per year. At flows of 0.1 MGD or greater, the following equation was used to calculate O&M hours:

$$\text{O\&M Hours} = 313.8\ (\text{FLOW})^{0.2925} \qquad (10\text{-}4)$$

where: FLOW = Facility flow rate, MGD

Groundwater sampling and analysis costs were developed based on the estimated cost for field sampling and vendor quotes for sample analyses.

Sludge removal costs were based on literature references, and sludge disposal costs were based on vendor quotes. Table 10-1 presents these unit costs.

10.3.6 Cyanide Destruction Treatment

The technology basis for cyanide destruction is hydrogen peroxide treatment. This technology is used by Facility 30542 and represents the basis of the treatment

performance data used by EPA to develop the limitation for cyanide. The system designed and costed by the cost model has a greater degree of control than the system used by Facility 30542, in that laboratory analysis of treated batches of wastewater for cyanide is required prior to discharge. This approach minimizes the potential for releases of wastewater with cyanide concentrations above the proposed limitations. Facility 30542 currently uses a qualitative field technique to measure cyanide after treatment which does not provide the same level of precision and accuracy as the EPA-approved analytical method.

The cyanide destruction treatment system costed for the pharmaceutical manufacturing industry includes the following equipment: four pumps (influent, effluent, sodium hydroxide, and hydrogen peroxide feed pumps), five tanks (pH adjustment, reactor, hydrogen peroxide feed, sodium hydroxide feed, and treated wastewater storage), two agitators (for the reactor and pH adjustment tanks), and a pre-engineered building to house the treatment unit. If the required volumes of the chemical additives were less than 5.7 gal/day, 55-gallon drums are used for storage instead of storage tanks.

10.3.6.1 Overview of Costing Methodology

Costs for in-plant cyanide destruction treatment were included for all facilities that reported the presence of cyanide in their wastewater in the Detailed Questionnaire. In-plant streams are defined as cyanide-bearing wastewater streams prior to dilution with noncyanide-bearing wastewater. Facilities that had portions of the technology basis for this treatment already on site were given credit for these elements, and therefore did not incur costs associated with a complete, new treatment system.

10.3.6.2 Design Bases and Assumptions

Cyanide destruction treatment is based on the reaction of cyanide with hydrogen peroxide under basic conditions to form ammonia and carbonate ions. Components that

comprise the treatment system were selected based on the system used by Facility 30542. The cost estimates generated by the cost model are based on the following treatment steps:

- Collection of the wastewater in the pH adjustment tank.
- Addition of sodium hydroxide to raise the pH in the tank.
- Transfer of wastewater to the reactor vessel.
- Addition of hydrogen peroxide to the reactor to treat cyanide, followed by field cyanide analysis.
- If the batch fails the field analysis, it is reacted again with additional hydrogen peroxide. If it passes, the wastewater is transferred to the storage tank for laboratory analysis.
- If the batch fails laboratory analysis, it is returned to the hydrogen peroxide reaction vessel for additional treatment. If it passes, it is discharged to the end-of-pipe treatment system (if applicable).

Costs for equipment and chemicals are based on vendor information.

The following key assumptions and design bases were used to cost cyanide destruction treatment:

- There is adequate land to install the treatment unit at each facility requiring cyanide destruction;
- All equipment is sized based on in-plant flow rate reported for waste streams containing cyanide; and
- Cyanide destruction treatment is operated in a batch mode, with up to three batches treated per day.

10.3.6.2 Costing Methodology

The treatment system components were chosen based on the system used by Facility 30542. Unit costs for the following were obtained from vendors or costing reference manuals: spill containment drum pallets, pumps, tanks, agitators, earthwork for building installation, pre-engineered building purchase and installation, chemical purchases, and laboratory and field monitoring. Tables 10-1 and 10-2 present these unit costs.

The following are included in the direct capital cost calculated for each facility requiring cyanide destruction treatment:

- Tanks for pH adjustment, reaction, storage of hydrogen peroxide, storage of sodium hydroxide, and storage of treated wastewater prior to discharge;
- For smaller volumes (less than 5.7 gal/day), 55-gallon drums to store chemicals used for cyanide destruction, instead of tanks (if drums are used, drum spill containment pallets are included);
- Pumps for delivering influent wastewater to the system, removing effluent from the system, delivering hydrogen peroxide to the reaction tank, and delivering sodium hydroxide to the pH adjustment tank;
- Agitators in the reaction and pH adjustment tanks;
- Earthwork to prepare the site for installation of a pre-engineered building (earthwork includes the construction of curbs and dikes for spill containment); and
- A building to house the cyanide destruction treatment system.

Table 10-3 presents the factors for calculating ancillary direct and all indirect capital costs.

The following are included in the total O&M costs calculated for each facility:

- O&M labor (assumed to be 1 hour per day);
- Materials and supplies;
- Chemical purchases;
- Field monitoring for cyanide concentration;
- Laboratory monitoring for cyanide concentration; and
- Electricity usage.

Maintenance material and supply costs are calculated based on the following relationships to installed equipment costs: 1% is used for pumps, 2% is used for storage tanks, and 5% is used for reaction tanks and agitators. Maintenance of pumps is also assumed to require one hour per day of operator labor.

Field and laboratory monitoring are assumed to occur once per batch for cyanide destruction treatment. Table 10-1 lists unit costs for cyanide monitoring. Electricity costs are based on pump usage.

10.3.7 Steam Stripping and Distillation

Steam stripping and distillation are used to treat organic pollutants and ammonia in wastewater. In a steam stripping column, the wastewater to be treated is introduced near the top of the column and is allowed to flow downward through the column by gravity. Steam is simultaneously introduced at the bottom of the column, and flows countercurrently to the wastewater. In a distillation column, the wastewater feed enters lower down the column to provide for a rectification section above the feed. In the rectification section, a portion of the condensed vapors are refluxed to the column to countercurrently contact the rising vapors. This process concentrates the volatile components in the overhead stream. In both steam stripping and distillation columns, organic compounds and ammonia enter the vapor phase as the steam contacts the wastewater, and are carried out of the top of the column with the steam. The column

overheads are condensed from vapor to liquid. A portion of the condensed overheads are returned to the top section of the column as reflux, the remaining portion is disposed of off-site. If the condensed overheads form an aqueous and organic layer, a decanter is used so that the portion returned to the column is the aqueous layer, while the portion disposed of is the organic layer. Treated wastewater exits the column from the bottom.

The following equipment is assumed to be required to perform steam stripping or distillation: stripping or distillation column, feed preheater/bottoms cooler, steam condenser, subcooler, decanter, air pollution control device, feed collection and storage tank, and associated pumps, piping, and instrumentation. Multiple units may be required for any or all of the equipment listed above, due to high facility flow rates or if multiple process streams requiring steam stripping or distillation exist at a facility. The air pollution control device is costed as an acid scrubber if ammonia is present in the waste stream; otherwise it is costed as a carbon canister. Facilities may find that it is cost effective to route vents from the steam stripper or distillation unit to an existing incinerator or other air pollution control system. This approach was not costed as part of this effort because information on existing air pollution control systems was not available.

10.3.7.1 Overview of Costing Methodology

Facilities were costed for steam stripping or distillation of all process area wastewater with concentrations of regulated pollutants above the long-term mean treatment performance concentrations for the steam stripping and steam stripping with distillation options, provided in Section 8. Cost estimates are based on the installation of the technology at an in-plant location. An in-plant location is defined as prior to dilution by non-process wastewater, commingling with other process wastestreams not containing regulated pollutants at treatable levels, and any conveyance, equalization, or other treatment units which are open to the atmosphere.

Facilities were given credit for steam stripping or distillation on site if an existing column was used to treat organic pollutants in wastewater to concentrations below the long-term mean treatment performance concentrations for steam stripping or steam stripping with distillation. If steam stripping or distillation treatment existed on site that did not treat organics to these levels, effluent from the existing column was considered as influent to the new column to be costed. It may be possible for facilities to improve performance of existing steam stripping and distillation columns to meet the required levels. However, the facility-specific information provided in responses to the Detailed Questionnaire was not adequate to determine if this would be possible for individual cases. Therefore, new columns were costed for all facilities not meeting the long-term mean treatment performance concentrations. The modelled compliance costs for facilities able to optimize their existing steam stripping or distillation column performance will be higher than actual compliance costs.

Information reported in the Detailed Questionnaire was used to characterize waste streams at each facility. Facility flow diagrams and process area information were used to determine how many in-plant process area streams existed at each facility. Quantities of pollutants discharged to wastewater and flow rate information reported in the Detailed Questionnaire were used to determine which constituents were present in each stream and to calculate their respective concentrations.

10.3.7.2 Design Bases and Assumptions

The steam stripping and distillation systems designed and costed by the cost model are based on achieving sufficient treatment of the least strippable compound present in the process wastewater stream being treated. Strippability groups were created for the purpose of establishing the design bases for both steam stripping and steam stripping with distillation treatment. The strippability groups contain all regulated compounds and range from most easily stripped (Group 1) to not strippable at all (Group 8). Table 10-6 lists all regulated compounds by these strippability groups. The strippability groups for

steam stripping with distillation contain all regulated compounds and range from most easily stripped (Group 1) to not strippable at all (Group 7). Table 10-7 lists all regulated compounds by these strippability groups.

The least strippable compound is selected for a particular stream based on the following criteria:

- Only compounds with concentrations above the steam stripping or steam stripping with distillation long-term mean treatment performance concentration are considered;
- Only compounds in the least strippable group (excluding the nonstrippable group) of any compounds at the facility are considered; and
- Within the least strippable group, the compound with the lowest Henry's Law Constant is selected.

Design parameters for the steam stripping or distillation column are selected based on the least strippable compound and its concentration in the process wastewater to be treated. Key steam stripping and distillation design parameters are:

- K value - the volatility or equilibrium ratio for a contaminant in a vapor/liquid system at the temperature and pressure of the column.
- Number of equilibrium stages - the number of contact units in a column within which the concentration of components in the liquid phase is in equilibrium with the concentration of components in the vapor phase.
- Steam-to-feed ratio - the volume of steam required to treat a given volume of wastewater.

Table 10-8 lists the steam stripping design parameters for constituents in Groups 1 through 7 (no values are given for compounds in Group 8 because they are not considered treatable by steam stripping). Table 10-9 lists the steam stripping with

distillation design parameters for constituents in Groups 1 through 6 (no values are given for compounds in Group 7 because they are not considered treatable by steam stripping with distillation).

Process simulations were used to assist in establishing the cost module design basis in two ways:

1. Process simulations were used to develop process designs that would achieve the long-term steam stripping or stream stripping with distillation performance levels discussed in Section 8 for pollutants in each of the strippability groups; and

2. Simulations were also used to help estimate a typical K value for pollutants in each strippability group.

The key process design parameters which must be determined in order to develop accurate costs for a steam stripping or distillation system are the steam/feed ratio and the number of equilibrium stages. For each of the cost groups, typical numbers of equilibrium stages and feed/steam (L/V) ratios were determined using process simulations. Tables 10-8 and 10-9 show the stages and L/V used for each group for both the steam stripping and steam stripping with distillation options.

For Groups 1 through 3, the number of stages and L/V were determined by varying stages and L/V until the steam stripping or steam stripping with distillation long-term mean treatment performance concentration could be achieved for the industry average influent concentration of the least strippable compound in the strippability group. As Tables 10-8 and 10-9 show, for Groups 4 and above, the number of stages and L/V ratios were determined as a function of influent concentration of the least strippable compound in the group.

The model scans all pollutants in each stream at each facility for strippability group and for concentration. If any pollutants are above the steam stripping or steam stripping with

distillation long-term mean treatment performance concentration (depending on the option being costed) and are considered strippable, then treatment is costed for the stream. Wastewater streams within a facility are considered separately; therefore, a facility with four in-plant wastewater streams might have four steam stripping or distillation systems costed. The largest diameter column costed by the model is 15 feet. This limitation is based on the difficulty associated with transporting larger columns. If a column larger than 15 feet is required, multiple columns are costed.

It is assumed that facilities requiring steam stripping or steam stripping with distillation treatment will have adequate space within existing enclosed process buildings.

10.3.7.3 Costing Methodology

Design equations were obtained from engineering texts, ASPEN methodology, and input from design engineers. Most unit costs were obtained from algorithms found in Peters and Timmerhaus, Third Edition (12). Others were obtained from vendor quotes. Unit costs were included in the cost model for the following: packed and tray columns, storage tanks, condensers, decanters, subcoolers, air pollution control devices, and feed preheaters. These unit costs were developed using algorithms dependent on multiple variables, and are presented in the Pharmaceuticals Manufacturing Industry Cost Documentation Report, which can be found in the Administrative Record for the rulemaking. The following table shows the purchase costs for the smallest and largest size of each major component of the distillation treatment unit, as designed and costed for all pharmaceutical manufacturing facilities that responded to the Detailed Questionnaire:

Component	Smallest Unit		Largest Unit	
	Cost	Size	Cost	Size
Packed Column	$17,552	Diameter = 10 inches Height = 17 (ft)	$237,538	Diameter = 38 inches Height = 52 (ft)
Tray Column	$80,274	Diameter = 49 inches Height = 34 (ft)	$1,185,637	Diameter = 175 inches Height = 87 (ft)
Condenser and Subcooler	$3,360	Surface area = 9.2 (ft^2)	$1,158,535	Surface area = 23,893 (ft^2)
Decanter	$119	Volume = 0.03 (ft^3)	$32,925	Volume = 3,788 (ft^3)
Acid Scrubber	$16,507	Diameter = 10 (inches)	$35,564	Diameter = 11 (inches)
Feed Preheater	$3,361	Surface area = 10.1 (ft^2)	$292,097	Surface area = 8,913 (ft^2)

These costs are for individual components only, some systems may require the installation of multiple components. Pump costs and chemical additive costs were obtained from vendor quotes. These unit costs are presented in Tables 10-1 and 10-2.

The following are included in the total capital cost calculated for each facility requiring steam stripping or distillation treatment:

- Stainless steel column(s), including either packing or trays (packing was used for columns with diameters less than 48 inches; trays were used for larger diameter columns);
- Stainless steel feed preheater(s)/bottoms cooler(s) to prepare influent wastewater for treatment and to maintain an acceptable temperature in the effluent from the column;
- Stainless steel steam condenser(s)/subcooler(s) to convert overheads from vapor to liquid;

- Decanter(s) to separate distilled organic compounds from water to be returned to the column;
- Air pollution control device(s) to remove noncondensible organics or ammonia from the vent stream;
- Stainless steel feed collection and storage tanks with capacities ranging from 12 to 24 hours; and
- Pumps to deliver influent wastewater to the column, refluxed wastewater back to the column inlet, and sodium hydroxide to the feed storage tank if pH adjustment is necessary (pH adjustment is required for streams that contain ammonia; stripping is performed at a pH of 8 for ammonia-bearing streams).

Stainless steel components were costed because of the corrosion potential of pharmaceutical manufacturing wastewater. Hastelloy was considered as a construction material, and may be necessary on a site-specific basis. However, for the purpose of calculating industry-wide costs, stainless steel was considered the most appropriate construction material.

Table 10-3 lists the factors that are used by the model to account for ancillary direct and all indirect capital costs.

The following are included in the O&M costs calculated for each facility:

- O&M labor;
- Steam usage;
- Chilled water usage for the condenser and subcooler;
- Hydrochloric acid addition to the ammonia scrubber (if necessary) or carbon canister replacement for air pollution control;
- Sodium hydroxide addition, if pH adjustment is necessary;

- Hauling and disposing of waste hydrochloric acid (if any) and waste solvents decanted from the column overhead stream;
- Miscellaneous O&M materials and supplies (assumed to be equal to 4% of the total capital cost); and
- Electricity usage.

O&M labor requirements are based on 12 labor hours per day to properly operate and maintain the steam stripping or distillation unit. Steam usage is calculated based on the facility flow rate and the selected steam-to-feed ratio.

Hydrochloric acid usage in the ammonia scrubber is calculated based on the amount of ammonia in the overhead stream from the column. It is assumed that 20% of the ammonia removed from the waste stream will be vented to the air pollution control device, and that the mass (pounds) of hydrochloric acid required will be 2.12 times the mass of the removed ammonia. The value 2.12 is based on the reaction of hydrochloric acid with ammonia in the air pollution control device. Carbon canister usage is based on the total mass of organic compounds removed from the waste stream. Based on ASPEN simulations, it is assumed that 0.29% of the overheads from the column will be vented to the air pollution control device. Based on EPA data from air emission studies at Superfund sites, it is assumed that 10 pounds of carbon will be required for each pound of organics removed in the air pollution control device.

Sodium hydroxide usage is calculated based on the presence of ammonia in the waste stream and the flow rate of the stream. Hauling and disposing of waste hydrochloric acid and waste solvents is based on unit costs displayed in Table 10-1. Electrical usage is calculated based on pump usage and pump horsepower.

10.3.8 Activated Carbon Adsorption

Activated carbon adsorption is used to remove organic constituents from wastewater. The organic constituents bind to sites on the activated carbon as the wastewater passes through beds containing the treatment medium. These organic constituents can be measured in bulk as COD. There are two primary types of activated carbon, granular and powdered. The cost estimates developed for the pharmaceutical manufacturing industry are based on the use of granular activated carbon (GAC) systems.

The system designed consists of three activated carbon beds operated in series, preceded by a multimedia filtration unit to capture solids that might prematurely foul the carbon beds. Multimedia filtration treatment is discussed in Section 10.3.4 and will not be described further in this section. The three-bed configuration allows for less wasted activated carbon than a more traditional, two-bed system because the first bed can be left in operation longer and allow a higher percentage of the activated carbon in the bed to be used before regeneration is required.

The equipment required to perform GAC treatment is assumed to include:

- An influent holding tank;
- An influent pump;
- Three carbon beds installed in series;
- A backwash pump;
- Two backwash tanks (one for backwash feed, and one for backwash settling); and
- A pre-engineered building for the three largest GAC systems. It is assumed that adequate floor space already exists to install the smaller, drum-based GAC systems.

10.3.8.1 Overview of Cost Methodology

No credit is given to facilities for having GAC treatment existing on site. All facilities requiring GAC treatment, based on comparison to long-term mean performance levels for GAC, are costed for new GAC treatment units.

10.3.8.2 Design Bases and Assumptions

There are four key design parameters for GAC treatment: empty bed residence time, saturation loading, hydraulic loading rate, and facility flow rate. These parameters are described below:

- Empty bed residence time (EBRT) - the time that the wastewater is in contact with the activated carbon. The assumed EBRT for all facilities is 45 minutes.
- Saturation loading - the mass of pollutant measured as COD (pounds) adsorbed per mass of carbon (pounds). This value is assumed to be 0.09066 pounds of pollutant per pound of carbon for all facilities. This saturation loading is based on GAC performance data gathered from the 1984 GAC pilot study.
- Hydraulic loading rate - the flow rate of wastewater per GAC bed surface area (gpm/ft^2). This number has been calculated from industry averages to be approximately 2.5 gpm/ft^2 for Subcategory A and C facilities and 3.0 gpm/ft^2 for Subcategory B and D facilities.
- Facility flow rate - This flow rate is used to size all equipment used by the activated carbon system.

The amount of carbon required over the course of a year for a given facility is calculated as follows. The reported COD concentration for a facility reported in the Detailed Questionnaire is compared to the GAC long-term mean performance level (for options that include advanced biological treatment, the COD concentration after advanced

biological treatment is compared to the GAC long-term mean performance level). The difference between the two concentrations is assumed to be the total organic load on the activated carbon. This concentration difference is converted to a mass using the reported facility flow rate. The mass and saturation loading are then used to calculate the total mass of carbon required per year to perform wastewater treatment.

It is assumed that facilities requiring activated carbon treatment have the available space necessary to implement this treatment technology.

10.3.8.3 Cost Methodology

Unit costs for the following were obtained from vendors: pumps, tanks, GAC systems, backwash systems, breakthrough monitoring, and carbon regeneration. Unit costs are provided in Tables 10-1 and 10-2.

The following are included in the total capital cost for each facility requiring GAC treatment systems (all equipment costs include purchase and installation):

- Multimedia filtration treatment unit directly upstream of the GAC unit.
- Feed tank with a 12-hour retention time for equalizing flow prior to introduction to the GAC treatment system.
- Feed pump to convey wastewater from the feed tank to the treatment system.
- The activated carbon treatment beds. Varying sizes of drums or tanks are used to hold the activated carbon. These units are pre-engineered with influent and effluent ports to allow easy hook up to facility piping.
- The backwash system, including two holding tanks and one pump. The backwash system operates by pumping clean facility water to the backwash tank, and then pumping water from the tank up

through the beds (in the opposite direction of normal wastewater flow) and into the backwash settling tank. Backwash water and solids are returned to the biological treatment unit, if available. If a biological system does not exist on site, decanted water is sent to the head of the treatment works and solids are taken off site for disposal.

- A pre-engineered building to house the activated carbon treatment system (only required for the three-tank-based systems).

Table 10-3 lists the factors for calculating ancillary direct and all indirect capital costs.

The following are included in the O&M costs calculated for each facility:

- O&M labor;
- Regeneration of spent activated carbon;
- Monitoring for breakthrough between carbon beds;
- Electricity usage; and
- Miscellaneous O&M materials and supplies (assumed to be 4% of the total capital cost).

Operation and maintenance labor is based on a curve with an assumed maximum required daily labor requirement of 4 hours (this maximum applies to facilities with flow rates above 500,000 gal/day). The equation used to calculate labor hour requirements is as follows:

$$\text{LABOR HOUR REQUIREMENTS} = [363.23 + (3.2347 \times (\text{FLOW})) - (0.0036842 \times (\text{FLOW})^2)] \times (\text{DAYS}) \quad (10\text{-}5)$$

where: FLOW = Facility flow rate, gpm
DAYS = Number of operating days per year.

Regeneration costs for spent carbon and monitoring costs were based on vendor quotes (33,16). Electricity usage was based on pump usage and pump horsepower.

10.3.9 Contract Hauling

Cost estimates for contract hauling of wastewater were developed for facilities with low flows. The treatment consists of storing untreated wastewater at the current end-of-pipe discharge point, and then hauling it off site for incineration. It has been determined that this approach is more cost-effective than other in-plant or end-of-pipe treatments for flows below 30 gallons per day.

The equipment required to perform this treatment depends on whether drums or a storage tank are used to store the wastewater. For drum storage, the only equipment required is the drums. If a storage tank is used, the equipment includes the tank and a discharge pump. It is assumed that for each scenario, the facility will have enough existing space for wastewater storage, requiring no additional land or facility improvement costs.

10.3.9.1 Overview of Costing Methodology

No credit was given to facilities for existing treatment on site. It was assumed that contract hauling would be performed at facilities with discharge flows below 30 gal/day and regulated pollutants at concentrations above the long-term mean treatment performance, regardless of the existing level of treatment.

10.3.9.2 Design Bases and Assumptions

The following assumptions were made for costing contract hauling:

- Facilities with zero wastewater discharge, no regulated pollutants reported, or no concentrations of regulated constituents above limitations did not incur any costs.
- Wastewater from all facilities requiring contract hauling required incineration.
- Any facility with a flow rate greater than 30 gal/day was not considered.
- The incineration facility was assumed to be 500 miles from the generating facility.

The selection of drums versus a storage tank for on site storage prior to disposal is based on the on-site storage time required to generate 5,000 gallons of wastewater. If it takes longer than 45 days to accumulate 5,000 gallons on site (approximately 110 gal/day), drums are used to store the wastewater. If it takes less than 45 days to generate 5,000 gallons, a storage tank is used instead.

Spill prevention for the drum storage system is provided by including spill prevention drum pallets for the storage area. These pallets provide a contained space beneath the drums to collect any leakage or spills.

10.3.9.3 Cost Methodology and Assumptions

Required costs for the following were obtained from vendor information: tanks, pumps, hauling, incineration, drums, and spill prevention pallets. Tables 10-1 and 10-2 present these unit costs.

The following were included in the total capital cost for each facility requiring contract hauling:

- Storage tank purchase and installation, if necessary (assumed to be an 11,000-gallon tank); and
- Discharge pump purchase and installation (assumed to be a 70-gpm pump), if necessary.

The following items are included as O&M costs for contract hauling:

- Drum purchase, if necessary;
- Spill prevention pallet purchase, if necessary;
- Electricity requirements for the pump, if necessary;
- Tank or drum area daily inspection (15 minutes per day);
- Loading and unloading of wastewater for transport;
- Transport of wastewater to the disposal facility (assumed to be 500 miles); and
- Incineration of the wastewater.

10.3.10 Compliance Monitoring

Compliance monitoring costs were calculated for all pharmaceutical manufacturing facilities that discharge wastewater. Costs represent analytical analysis costs based on which pollutants were reported in 1990 to be present in a facility's wastewater. Monitoring may be required in plant, at the end of pipe, or in both locations, depending on the regulatory option. See Sections 13 through 17 for additional detail on monitoring locations.

Costs for monitoring the discharge levels of BOD_5, COD, and TSS have not been included, as no incremental costs above those which the plants are presently incurring are anticipated. Cyanide monitoring costs are included as part of the cyanide treatment cost module and are not calculated in the monitoring module. It is assumed that no additional physical equipment is required to perform monitoring.

10.3.10.1 Overview of Costing Methodology

For the purpose of selecting in-plant or end-of-pipe monitoring, four scenarios related to regulatory options were considered:

1. Options with no steam stripping or steam stripping with distillation (no in-plant treatment of organics);

2. Options with in-plant steam stripping or steam stripping with distillation and no end-of-pipe treatment;

3. Options with in-plant steam stripping or steam stripping with distillation, and end-of-pipe treatment that does not include activated carbon treatment; and

4. Options with in-plant steam stripping with distillation and activated carbon treatment.

The following paragraphs describe the cost estimates for monitoring under each of these scenarios.

Options With No Steam Stripping or Steam Stripping with Distillation

Regulatory options that did not include any in-plant steam stripping or steam stripping with distillation treatment were costed for weekly end-of-pipe (EOP) monitoring for compounds present at the facility and one annual EOP full analytical scan for all regulated pollutants.

Options With In-Plant Steam Stripping or Steam Stripping with Distillation and No End-of-Pipe Treatment

Regulatory options that included in-plant steam stripping or steam stripping with distillation but no EOP treatment were costed for weekly monitoring at each in-plant monitoring point for compounds present in that facility stream and full analytical scans for all regulated pollutants at each in-plant monitoring point annually.

Implementation of the proposed PSES and PSNS options will include standards at both in-plant and end-of-pipe locations. Insufficient time was available to incorporate this implementation approach prior to completion of the costs for proposal. This modification will be addressed in the costs estimates supporting the promulgated rulemaking.

Options With In-Plant Steam Stripping or Steam Stripping with Distillation and End-of-Pipe Treatment that Does Not Include Activated Carbon Treatment

Regulatory options that included in-plant steam stripping or steam stripping with distillation and EOP treatment, not including activated carbon treatment, were costed for a combination of in-plant and EOP monitoring. Weekly in-plant monitoring was costed for compounds considered treatable by steam stripping or steam stripping with distillation in the facility stream(s). Weekly EOP monitoring was costed for compounds considered not to be treatable by steam stripping or distillation present at the facility. One annual EOP full analytical scan for all regulated compounds was also costed.

The proposed BAT option for Subcategory A and C operations and the proposed NSPS options include limitations at the end-of-pipe location only. However, it is likely that facilities will also incur costs for in-plant monitoring, as they conduct routine internal monitoring to access whether their steam stripping and distillation system are performing as intended.

Options With In-Plant Steam Stripping with Distillation and Activated Carbon Treatment

Regulatory options that included in-plant distillation and EOP activated carbon treatment were costed for a combination of in-plant and EOP monitoring. Weekly in-plant monitoring was costed for compounds considered to be not treatable by activated carbon. Weekly EOP monitoring was costed for compounds considered to be treatable by activated carbon. One annual EOP full analytical scan for all regulated compounds was also costed.

Under each scenario described above, analytical methods were selected to detect all compounds reported to be present in facility waste streams.

10.3.10.2 Cost Methodology

There are no capital items associated with compliance monitoring. The only O&M costs included for this activity are the laboratory analytical costs. It is assumed that the labor required to perform monitoring sampling is negligible compared to labor requirements already existing at each facility. It is also assumed that any materials required for monitoring are already present at the facility or are provided by the laboratory performing the analyses.

All analytical cost information was provided by vendors of analytical services.

10.4 Engineering Costs by Regulatory Option

Table 10-10 presents a summary of estimated BPT, BCT, BAT, and PSES engineering costs, broken down by subcategory, discharge type, and regulatory option. Costs shown include capital and operation and maintenance (including energy usage) costs totaled for each group of applicable facilities.

It should be noted that advanced biological treatment costs are incorporated into both the BPT and BAT costs for direct dischargers. Facilities would install only one treatment system adequate to comply with both BPT and BAT limitations. Therefore, the BPT and BAT costs should not be summed as this would create double counting for the biological treatment costs, rather a facility would incur the BAT costs in complying with both BAT and BPT.

For NSPS and PSNS, costs were developed using the existing facility information to model potential new source facilities. NSPS and PSNS costs were developed on an annualized basis using amortized yearly costs and assuming a Subcategory A and/or C facility flow rate of 1 MGD and a subcategory B and/or D facility flowrate of 0.1 MGD.

The amortized yearly costs are equal to the sum of amortized capital costs and the yearly operation and maintenance costs. The capital costs are amortized using the following equation:

$$\text{Amortized Capital Cost (\$/yr)} = \text{Capital Cost (\$)} \left[\frac{i\,(1+i)^n}{(1+i)^n - 1} \right]$$

where: i = Interest rate of 0.114
n = Equipment life of 20 years.

Table 10-11 presents a summary of estimated NSPS and PSNS engineering costs on an amortized yearly basis.

Table 10-1

Operation and Maintenance Unit Costs Used By the Cost Model

Unit Disposal Costs			
Activity	**Cost (1990 $)**	**Units**	**Reference**
Incinerate drums of liquid waste	480.10	55-gallon drum	[2]
Dispose of bulk wastewater	5.02	gallon	(2)
Incinerate solvents in bulk	140.00	ton	[3,4]
Incineration of waste HCL	180.00	ton	(4)
Dispose of biological treatment sludge	50.00	ton	[5] (a)
Unit Hauling Costs			
Activity	**Cost (1990 $)**	**Units**	**Reference**
Haul solvents	29.02	ton	(4)
Haul drums/bulk wastewater	2,626.00	full load (80 drums or 5,000 gallons bulk liquid)	(2)
Haul biological treatment sludge	4.05	loaded mile	[6]
Unit Chemical Costs			
Chemical	**Cost (1990 $)**	**Units**	**Reference**
NaOH (50%)	310.00	ton	[7]
H_2O_2 (50%)	0.495	pound	(7)
Nitrogen (Ammonium Sulfate)	0.013	pound	(7)
Phosphorous (Phosphoric Acid)	0.199	pound	(7)
Hydrochloric acid	395.77 - 482.65	drum (500 lbs)	[8]
Polymer	2.25	pound	[9]
Miscellaneous Unit Costs			
Item	**Cost (1990 $)**	**Units**	**Reference**
O&M labor rate	27.74	hour	[10]
Electricity usage fee	0.04	kilowatt-hour	[11]
Steam	3.20	1000 lbs	[12]

Table 10-1
(Continued)

Miscellaneous Unit Costs			
Item	**Cost (1990 $)**	**Units**	**Reference**
Sample fee (for off-site disposal)	322.22	per load of wastewater	(2)
Drum purchase	43.66	drum	13
Dredge polishing pond sludge	6.95	cubic yard	14
Field cyanide analysis	0.50	per sample	15
Laboratory cyanide analysis	27.50	per sample	16

(a) Unit cost was calculated by taking the median of costs reported by pharmaceutical manufacturing facilities for disposing of similar wastes.

Table 10-2

Capital Unit Costs Used by the Cost Model

Construction Unit Costs			
Activity	**Cost (1990 $)**	**Units**	**Reference**
Excavation	4.81	cubic yard	[17]
Concrete wall installation	547.69	cubic yard	[18]
Concrete slab installation	120.51	cubic yard	(18)
Prefabricated building installation	19.51	square foot of floor space	[19]
Impermeable, double liner installation	3.58	square foot	[20]
Crane rental	98.15	hour	[21]
Handrail installation	46.91	linear foot	[22]
Purchased, Installed Treatment Equipment Unit Cost			
Item	**Cost (1990 $)**	**Standard Size**	**Reference**
Package biological treatment plant	67,944	100,000 gal/day	(22)
Clarifier	139,610	90 ft diameter	(22)
Filtration unit	307,143	784 ft^2 of filter surface area	(22)
Fix-mounted surface aerator	33,080	20 HP	[23]
Pump station pump (large applications)	32,110	3,000 gpm	(22)
Filter press (1 ft^3 to 20 ft^3)	6,119 to 30,992	per press	[24]
Sludge Thickening Tank (100 gal to 500,000 gal)	1,270 to 79,062	per tank	[25]
Miscellaneous Unit Capital Costs			
Activity/Item	**Cost (1990 $)**	**Units/Standard Size**	**Reference**
Drum pallet (spill preventative)	338.64	4-drum pallet	[26]
Monitoring well installation	4,444	per well	[27]

Table 10-2

(Continued)

Miscellaneous Unit Capital Costs			
Activity/Item	**Cost (1990 $)**	**Units/Standard Size**	**Reference**
Closure plan development	28,393	per polishing pond	[28]
Groundwater background concentration determination	114,868	per acre of polishing pond	(27)
RCRA Part B Permit Application	118,303	per polishing pond	(28)
Develop a groundwater monitoring plan	7,763	per polishing pond	(27)
Unit Capital Costs Using Curves or Ranges			
Item/Activity	**Range/Equation**	**Units**	**Reference**
Small pumps (3 - 27 gpm)	Cost = 45.705 (Q) + 615.24 (Q= flow in gpm)	per pump	[29]
Larger pumps (50 - 900 gpm)	Cost= 6.09 (Q) + 2,485 (Q = flow in gpm)	per pump	(23)
Carbon steel tanks (11,000 to 150,600 gal)	Cost = 0.1935(V) + 8814 (V = volume in gallons)	per tank	[30]
Floating aerators (20 HP to 100 HP)	11,698 to 42,662	per aerator	[31]
Package filtration unit (SA < 400 ft^2)	Cost = $60,034(SA)^{0.3203}$ (SA = filter surface area in square feet)	per filter unit	(22)
Reaction vessel agitator (0.25 to 5.0 HP)	1,210 to 2,614	per agitator	[32]
Activated carbon treatment systems (165 lbs to 40,000 lbs of carbon)	495 to 250,000	per system	[33]

Table 10-3

Factors Used To Calculate Indirect and Ancillary Direct Capital Costs As a Percentage of Total Purchased and Installed Capital Cost

Technology	Factor (%)	Reference
Equalization	5	(22)
Package aeration (flow ≤ 0.5 MGD)	11	(22)
Full-size aeration (flow > 0.5 MGD)	11	(22)
Clarification	18	(22)
Multimedia filtration	25	(22)
Polishing pond treatment	11	(22)
Cyanide destruction	35	[34]
Distillation	62.5	(12)
Activated carbon treatment	42	(2)

Table 10-4

Constants and Values Used to Model Biological Treatment

Parameter	Subcategory A and C Value	Subcategory B and D Value	Units
Temperature	24.56	24.56	°C
Synthesis oxygen coefficient	1.05	1.05	lb O_2/lb BOD_5
Influent VSS/TSS ratio	0.65	0.65	NA
Nondegradable influent VSS	0.70	0.70	NA
Clarifier hydraulic loading	400	400	gal/day/ft^2
Clarifier solids loading	20	20	lb/day/ft^2
Clarifier polymer addition	1.5	1.5	mg/L
Field oxygen transfer	3.0	3.0	lb/HP-hr
Substrate removal rate constant (K)	11.14	2.06	NA
Synthesis yield coefficient	0.36	0.78	NA
Endogenous decay rate constant	0.0	0.0	NA
BOD_5 associated with effluent TSS	0.23	0.24	mg/mg
COD removed to BOD_5 removed ratio	0.615	0.52	NA

NA - Not applicable.

Source: Mean values based on information provided in the Detailed Questionnaire.

Table 10-5

Operation and Maintenance Labor Hour Calculations for Biological Treatment

Activity	Type of Labor	Minimum hours (per year)	Equation(s) for calculating hours per year
Package aeration	Operation	1200	$1683\ (FLOW)^{0.1469}$
	Maintenance	640	$1143\ (FLOW)^{0.2519}$
Full-size aeration	Operation	NA	$242.4\ (TICA)^{0.3731}$ (TICA < 200) $100\ (TICA)^{0.5425}$ (TICA ≥ 200)
	Maintenance	NA	$106.3\ (TICA)^{0.4031}$ (TICA < 100) $42.6\ (TICA)^{0.5956}$ (TICA ≥ 100)
Clarification	Operation	350	$37.1(SA)^{0.3247}$ (1,000 ≤ SA ≤ 3,000) $4.0\ (SA)^{0.6020}$ (SA > 3,000)
	Maintenance	200	$30.3\ (SA)^{0.2733}$ (1,000 ≤ SA ≤ 3,000) $2.05\ (SA)^{0.6098}$ (SA > 3,000)
Sludge Handling	Operation	NA	1 hour per batch per press for presses < 6 ft^3 2 hours per batch per press for presses between 6 ft^3 and 12 ft^3 3 hours per batch per press for presses larger than 12 ft^3 The maximum number of operation hours per day at any one facility is 27.
	Maintenance	NA	2 hours per year per press

FLOW - Facility end-of-pipe wastewater treatment flow (MGD).
TICA - Total installed capacity of aeration (horsepower).
SA - Clarifier surface area (ft^2).
NA - Not applicable.

Table 10-6

Steam Stripping Strippability Groups for All Regulated Compounds

Compound	Strippability Group	Compound	Strippability Group
n-Heptane	1	Amyl alcohol	5
Cyclohexane	2	2-Butanone (MEK)	5
Benzene	3	tert-Butyl alcohol	5
Chlorobenzene	3	Dimethylamine	5
Chloroform	3	N,N-Dimethylaniline	5
1,2-Dichloroethane	3	Formamide	5
Diethyl Ether	3	Furfural	5
Isopropyl Ether	3	Isopropanol	5
Methyl Cellosolve	3	Methylamine	5
Methylene Chloride	3	2-Methylpyridine	5
Xylenes	3	Acetone	5
Ammonia	4	Aniline	6
Chloromethane	3	n-Butyl alcohol	6
o-Dichlorobenzene	3	1,4-Dioxane	6
n-Hexane	1	Ethanol	6
Toluene	3	n-Propanol	6
Trichlorofluoromethane	2	Pyridine	5
n-Amyl Acetate	4	Methanol (Methyl alcohol)	7
n-Butyl Acetate	4	Petroleum naphtha	7
Diethylamine	4	Acetonitrile	8
Ethyl Acetate	4	N,N-Dimethylacetamide	8
Isobutyraldehyde	4	N,N-Dimethylformamide	8
Isopropyl Acetate	4	Dimethyl sulfoxide	8
Methyl Formate	4	Ethylene glycol	8
MIBK	4	Formaldehyde	8
Tetrahydrofuran	4	Phenol	8
Triethylamine	4	Polyethylene glycol 600	8

Table 10-7

Steam Stripping with Distillation Strippability Groups for All Regulated Compounds

Compound	Strippability Group	Compound	Strippability Group
n-Heptane	1	Amyl alcohol	5
n-Hexane	1	Aniline	5
Cyclohexane	2	2-Butanone (MEK)	5
Trichlorofluoromethane	2	n-Butyl alcohol	5
Benzene	3	tert-Butyl alcohol	5
Chlorobenzene	3	Dimethylamine	5
Chloroform	3	N,N-Dimethylaniline	5
Chloromethane	3	1,4-Dioxane	5
o-Dichlorobenzene	3	Ethanol	5
1,2-Dichloroethane	3	Formamide	5
Diethyl Ether	3	Furfural	5
Isopropyl Ether	3	Isopropanol	5
Methyl Cellosolve	3	Methylamine	5
Methylene Chloride	3	2-Methylpyridine	5
Toluene	3	n-Propanol	5
Xylenes	3	Acetone	5
Ammonia	4	Pyridine	5
n-Amyl Acetate	4	Methanol (Methyl alcohol)	6
n-Butyl Acetate	4	Petroleum naphtha	6
Diethylamine	4	Acetonitrile	7
Ethyl Acetate	4	N,N-Dimethylacetamide	7
Isobutyraldehyde	4	N,N-Dimethylformamide	7
Isopropyl Acetate	4	Dimethyl sulfoxide	7
Methyl Formate	4	Ethylene glycol	7
MIBK	4	Formaldehyde	7
Tetrahydrofuran	4	Phenol	7
Triethylamine	4	Polyethylene glycol 600	7

Table 10-8

Steam Stripping Design Parameters Established by Strippability Group

Strippability Group	Concentration of Least Strippable Contaminant	K Value	Number of Equilibrium Stages	Feed-to-Steam Ratio
1	ALL	10,219	4	12.0
2	ALL	1874.2	4	12.0
3	ALL	400	6	12.0
4	< 2,000	44.5	8	12.0
	> 2,000	44.5	10	12.0
5	≤ 1,000	21.6	10	12.3
	1,000 < conc. ≤ 5,000	21.6	14	12.9
	5,000 < conc. ≤ 10,000	21.6	14	12.1
	10,000 < conc. ≤ 50,000	21.6	14	10.9
	> 50,000	21.6	14	9.7
6	< 1,000	11.5	14	12.0
	1,000 < conc. ≤ 5,000	11.5	14	8.8
	5,000 < conc. ≤ 10,000	11.5	14	7.9
	> 10,000	11.5	14	6.8
7	< 5,000	7.8	14	7.8
	5,000 < conc. ≤ 10,000	7.8	14	6.3
	10,000 < conc. ≤ 20,000	7.8	14	5.5
	20,000 < conc. ≤ 30,000	7.8	14	5.1
	> 30,000	7.8	14	4.6
8	NA	NA	NA	NA

conc. - Concentration in mg/L.
ALL - Compounds in Groups 1, 2, and 3 are considered very strippable; therefore, all expected influent concentrations can be treated to limitations using the design criteria listed.
NA - Compounds in Group 8 are not considered strippable; therefore, no design parameters are listed.

Table 10-9

Steam Stripping with Distillation Design Parameters Established by Strippability Group

Strippability Group	Concentration of Least Strippable Contaminant	K Value	Number of Equilibrium Stages	Feed-to-Steam Ratio
1	ALL	10,219	4	12.0
2	ALL	1874.2	4	12.0
3	ALL	400	6	10.0
4	< 10,000	31.6	10	10.0
	> 10,000	31.6	10	7.5
5	< = 100	11.5	14	6.0
	100 < conc. < = 1,000	11.5	14	5.0
	1,000 < conc. < = 10,000	11.5	14	4.0
	> 10,000	11.5	14	3.5
6	< = 100	7.8	14	4.0
	100 < conc. < = 1,000	7.8	14	3.3
	1,000 < conc. < = 10,000	7.8	14	3.0
	> 10,000	7.8	14	2.5
7	NA	NA	NA	NA

conc. - Concentration in mg/L.
ALL - Compounds in Groups 1, 2, and 3 are considered very strippable; therefore, all expected influent concentrations can be treated to limitations using the design criteria listed.
NA - Compounds in Group 7 are not considered strippable; therefore, no design parameters are listed.

Table 10-10

Summary of BPT, BCT, BAT, and PSES Engineering Costs

Subcategory	Regulation	Option	Capital Cost ($/yr)	O&M Cost ($/yr)
A and C	BPT	1	0	0
A and C	BPT	2	14,700,000	6,940,000
A and C	BPT	3	21,900,000	7,380,000
A and C	BPT	4	37,400,000	21,700,000
A and C	BPT	5	44,200,000	23,300,000
A and C	BCT	1	0	0
A and C	BCT	2	9,730,000	2,000,000
A and C	BCT	3	16,900,000	2,960,000
A and C	BCT	4	32,400,000	16,500,000
A and C	BCT	5	39,200,000	19,100,000
A and C	BAT	1	15,000,000	8,540,000
A and C	BAT	2	56,400,000	35,700,000
A and C	BAT	3	68,000,000	58,000,000
A and C	BAT	4	92,900,000	114,000,000
B and D	BPT	1	0	0
B and D	BPT	2	606,000	519,000
B and D	BPT	3	2,980,000	754,000
B and D	BCT	1	0	0
B and D	BCT	2	559,000	449,000
B and D	BCT	3	2,930,000	684,000
B and D	BAT	1	644,000	1,100,000
B and D	BAT	2	1,740,000	937,000
B and D	BAT	3	3,000,000	1,950,000
B and D	BAT	4	10,300,000	3,060,000
A and C	PSES	1	70,800,000	46,400,000
A and C	PSES	2	90,100,000	82,000,000
A and C	PSES	3	144,000,000	106,000,000
A and C	PSES	4	187,000,000	178,000,000
B and D	PSES	1	21,000,000	7,660,000
B and D	PSES	2	25,400,000	14,000,000
B and D	PSES	3	36,000,000	60,600,000

Table 10-11

Summary of NSPS and PSNS Engineering Costs

Subcategory	Regulation	Option	Annualized Costs ($/yr)	Costs at Set Flowrate (MGD)
A and C	NSPS	1	4,100,000	1
A and C	NSPS	2	14,200,000	1
B and D	NSPS	1	218,000	0.1
B and D	NSPS	2	336,000	0.1
A and C	PSNS	1	4,010,000	1
A and C	PSNS	2	4,990,000	1
B and D	PSNS	1	391,000	0.1
B and D	PSNS	2	454,000	0.1

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SECTION 11

REGULATORY OPTIONS SELECTION

11.1 Introduction

This section presents proposed regulatory options for the pharmaceutical manufacturing industry and discusses the factors considered in determining the selected options for BPT, BAT, NSPS, PSES, and PSNS. Factors considered included: reduction in pollutant discharges to the environment, costs to the industry, age of the equipment and facilities involved, the manufacturing processes used, process changes required, nonwater quality environmental impacts, engineering aspects of the control technologies, and energy requirements.

The regulatory options selected provide the technology basis of the effluent limitations guidelines and standards presented in Sections 13 (BPT), 15 (BAT), 16 (NSPS), and 17 (PSES and PSNS). Selection of the BCT option is determined by the BCT cost test analysis, which is discussed in Section 14. Owners or operators of facilities subject to these regulations would not be required to use the specific wastewater treatment technologies selected by EPA to establish the limitations and standards. Rather, a facility could choose to use any combination of process changes, water use changes, and wastewater treatment to comply with the limitations and standards provided that the limitations and standards are not achieved through prohibited dilution.

Sections 11.2 through 11.6 provide an overview of the regulatory options considered, the options selected as the bases of the proposed regulation, and the rationale for options selected under BPT, BAT, NSPS, PSES, and PSNS, respectively.

11.2 BPT

Effluent limitations guidelines based on the best practicable control technology currently available are generally based upon the average of the best existing performance, in terms of treated effluent discharged by facilities in a subcategory. BPT focuses on end-of-pipe treatment technology and such process changes and internal controls that are common industry practice. Based on Section 304(b)(1)(B) of the CWA, the factors considered in assessing BPT include:

- The cost of achieving effluent reductions in relation to the effluent reduction benefits;
- The age of equipment and facilities involved;
- The process used;
- Process changes required;
- Engineering aspects of the control technologies;
- Nonwater quality environmental impacts (including energy requirements); and
- Other factors the Administrator deems appropriate.

The BPT limitations proposed for the pharmaceutical manufacturing industry apply to direct dischargers and are intended to regulate BOD_5, COD, TSS, and cyanide. The Agency is not proposing to change the current BPT effluent limitations set for pH in the November 17, 1976 interim final regulation for the pharmaceutical manufacturing industry.

Thirty-one of the 38 direct discharging pharmaceutical manufacturing facilities currently use on-site activated sludge biological treatment as part of their wastewater treatment systems. Therefore, the Agency has evaluated this technology in addition to other

treatment techniques for BOD_5, COD, and TSS treatment performance. In addition, all of the BPT regulatory options include treatment for cyanide-bearing wastewaters at Subcategory A and C direct dischargers. The BPT regulatory options considered by the Agency are discussed in Section 7.3.2 and are listed below.

Regulatory Option	Control Technology Description
Subcategories A and C	
BPT Option 1	Current treatment systems (no cost option)
BPT Option 2	In-plant cyanide destruction, followed by end-of-pipe advanced biological treatment
BPT Option 3	In-plant cyanide destruction, followed by end-of-pipe advanced biological treatment and filtration
BPT Option 4	In-plant cyanide destruction, followed by end-of-pipe advanced biological treatment and polishing pond treatment
BPT Option 5	In-plant cyanide destruction, followed by end-of-pipe advanced biological treatment, filtration, and polishing pond treatment
Subcategories B and D	
BPT Option 1	Current treatment systems (no cost option)
BPT Option 2	End-of-pipe advanced biological treatment
BPT Option 3	End-of-pipe advanced biological treatment and filtration

Analysis of the impacts of these options in terms of reduction in pollutant discharges to the environment, costs to industry, and nonwater quality environmental impacts (including energy impacts) are described in Sections 9, 10, and 12, respectively. The Agency is proposing the options identified as Option 2 for Subcategories A and C and for Subcategories B and D, based on the comparison of estimated costs to effluent reduction benefits of each option. For all subcategories, Option 2 represents the most appropriate balance of costs and effluent reduction benefits and other factors.

11.3 BAT

Effluent limitations guidelines based on the best available technology economically achievable represent the best existing economically achievable performance of plants in

the industrial subcategory. The CWA establishes BAT as the principal national means of controlling the direct discharge of priority pollutants and nonconventional pollutants to waters of the United States. Based on Section 304(b)(2)(B) of the CWA, the factors considered in assessing BAT include:

- The age of equipment and facilities involved;
- The process used;
- Process changes required;
- Engineering aspects of control technologies;
- The cost of achieving effluent reduction;
- Nonwater quality environmental impacts (including energy requirements); and
- Other factors the Administrator deems appropriate.

The Agency retains considerable discretion in assigning the weight to be accorded these factors. BAT may include process changes or internal controls, even when these technologies are not common industry practice.

The BAT regulatory options considered by the Agency are discussed in Section 7.3.4 and are listed below.

Regulatory Option	Control Technology Description
Subcategories A and C	
BAT Option 1	In-plant cyanide destruction, followed by end-of-pipe advanced biological treatment with nitrification
BAT Option 2	In-plant steam stripping and cyanide destruction, followed by end-of-pipe advanced biological treatment
BAT Option 3	In-plant steam stripping with distillation and cyanide destruction, followed by end-of-pipe advanced biological treatment
BAT Option 4	In-plant steam stripping with distillation and cyanide destruction, followed by end-of-pipe advanced biological treatment and activated carbon adsorption

Regulatory Option	Control Technology Description
Subcategories B and D	
BAT Option 1	End-of-pipe advanced biological treatment
BAT Option 2	In-plant steam stripping followed by end-of-pipe advanced biological treatment
BAT Option 3	In-plant steam stripping with distillation followed by end-of-pipe advanced biological treatment
BAT Option 4	In-plant steam stripping with distillation followed by end-of-pipe advanced biological treatment and granular activated carbon adsorption

Analysis of the impacts of these options in terms of reduction in pollutant discharges to the environment, costs to industry, and nonwater quality environmental impacts (including energy impacts) are described in Section 9, 10, and 12, respectively. The Agency is proposing Option 2 as the proposed technology basis for BAT limitations for Subcategories A and C. The Agency is proposing Option 1 as the technology basis for BAT limitations for Subcategories B and D. The Agency's rationale for BAT selection is discussed below by subcategory.

11.3.1 Subcategories A and C

EPA selected Option 2 as the proposed technology basis for BAT limitations for facilities with Subcategory A and/or C operations because EPA believes this option represents the best available technology economically achievable, considering all statutory factors.

The Agency estimated that none of the options would result in any closures or unemployment. Based on these findings, EPA concluded that all four options are economically achievable. EPA selected Option 2 because it determined that option represented the best available technology from among all the economically achievable options.

The Agency found that the annual incremental increase in electrical power consumption for all facilities to achieve Option 2 was 13,200 MW. This increase is equivalent to an increase of approximately 0.25 percent of the pharmaceutical industry's purchased

electrical energy usage in 1990. Using the industry's 1990 purchased electrical energy usage on a baseline, the estimated incremental increases for electrical power consumption for the remaining options were, for Option 3, an increase of 13,800 MW and, for Option 4, an increase of 17,900 MW. With respect to energy needs associated with steam generation for steam stripping and distillation, the Agency found that Option 2 would result in 720,000 MW of incremental energy consumption, or approximately an 8 percent increase above the industry's 1990 total energy consumption. For Option 3, EPA found that 2,220,000 MW of incremental energy consumption, or a 25 percent increase above the industry's 1990 total energy consumption, would be required.

EPA did not select Option 3 as proposed BAT because of the large increase in energy consumption associated with this option. This decision is consistent with the CWA's requirement that EPA take into account energy requirements in selecting BAT. While steam generation under BAT Option 2 requires a higher energy consumption than the energy purchased by the industry in 1990, the Agency notes that the potential for solvent recovery and reuse will off-set these energy expenditures.

It should be noted that in estimating the energy consumption for steam generation associated with Options 2 and 3, EPA assumed, based on the available detailed questionnaire data, that very high volumes of wastewater would need to be stripped and distilled, thus requiring high demands for steam. EPA believes that this assumption is very conservative, because the Agency assumed from the Detailed Questionnaire responses that wastewater streams containing high concentrations of volatile organic pollutants could not be segregated from steams containing minimal or no concentrations of these pollutants. EPA believes that stream segregation is possible and expects that more recent data will show that the volume of wastewater that would be subject to steam stripping and/or distillation is substantially lower than the volume assumed in this proposal. Lower volumes would result in higher concentrations of the volatile organic pollutants to be stripped, less steam and thus less energy would be required to strip or distill such pollutants from low volume, high concentration wastewater.

The Agency considered other non-water quality environmental impacts of the selected option including:

- The role which the proposed regulation may play in minimization, recycle, and disposal of characteristic (ignitable) volatile organic wastes; and
- The effect of the options on the current levels of air emissions from wastewaters.

BAT Options 2 and 3 will generate 52,200 and 61,000 metric tons per year of condensates, respectively, due to the use of steam stripping and steam stripping with distillation. The condensates may include both halogenated and nonhalogenated solvents. Plants may choose to purify these condensates and then recycle/reuse the purified solvents as raw materials or use the condensate streams as fuel for incinerators or boilers either on or off-site. In the Agency's costing effort, EPA assumed all condensates will be disposed of by off-site incineration. The difference in off-site incineration costs between Options 2 and 3 is about 10 percent and this cost differential represents a small part of the total costs associated with these options. Therefore, EPA concluded that the generation of condensates as a result of steam stripping and steam stripping with distillation does not provide a basis for choosing between these options.

The Agency also considered the effect of the options on the current levels of air emissions from wastewater. EPA used the WATER7 computer model employed by the EPA Office of Air and Radiation (OAR) in the recently promulgated Hazardous Organic NESHAP (HON) for the Synthetic Organic Chemical Manufacturing Industry (SOCMI), in conjunction with the Detailed Questionnaire responses, to evaluate the 1990 levels of air emissions from wastewater for this industry. Direct discharging facilities with Subcategory A and/or C operations reported in the 1990 questionnaire that they emit from wastewater a total of 3.2 million pounds/year of volatile organic pollutants, and the WATER7 model projected 14 million pounds/year of those pollutants

from wastewater. The results of the analyses were used to estimate air emission increases or decreases for the regulatory options. The Agency estimated that Option 1 would result in a minimal increase in air emissions, while Option 2 and 3 would decrease air emissions by 5,300 and 6,350 metric tons per year, respectively. Option 4 would achieve the same air emission reduction as Option 3. In EPA's view, these beneficial non-water quality environmental impacts militate in favor of selecting a technology option employing steam stripping or distillation (Options 2, 3, or 4).

The Agency did not find that the age of equipment and facilities involved provided any basis for choosing among the options. The Agency also evaluated whether the engineering aspects of the options were compatible with the manufacturing processes employed and potential process changes at facilities with Subcategory A and/or C operations. EPA concluded that the engineering aspects of all four options were compatible with current manufacturing processes and possible process changes at these facilities, and the results of this evaluation did not provide a basis for selecting an option.

11.3.2 Subcategories B and D

EPA is proposing Option 1 as the technology basis for BAT limitations for facilities with Subcategory B and/or D operations because, on the basis of the data submitted by the direct dischargers in these subcategories, EPA determined that this technology basis is the best available technology economically achievable for these pollutants. In making the proposed BAT determination, EPA analyzed data for each facility identified through the 1989 Pharmaceutical Screener Questionnaire and the 1990 Detailed Questionnaire as engaging in Subcategory B and/or D operations. The results of the screener questionnaire indicate that, nationwide, 14 pharmaceutical manufacturing plants with direct discharges engage only in Subcategory B and/or D operations (excluding Subcategory E research activities). These 14 facilities reported to EPA in response to the 1990 Detailed Questionnaire that they discharge BOD_5, TSS, COD, six solvents and no priority pollutants. EPA's analysis of the questionnaire data indicates that the total

nonconventional pollutant loadings discharged, on average, for each facility with Subcategory B and/or D operations in 1990 was 1,660 pounds/year. In addition, these 14 facilities reported in their questionnaire responses that they emit from wastewater a total of 170 pounds/year of volatile organic pollutants. Subsequent analysis by EPA using its WATER7 model indicates that these 14 facilities may actually emit closer to 35,000 pounds/year from wastewater. By way of comparison, facilities with Subcategory A and/or C operations reported in the 1990 questionnaire that they emit from wastewater a total of 3.2 million pounds/year of volatile organic pollutants, and the WATER7 model projected 14 million pounds/year of those pollutants from wastewater.

In view of the comparatively small quantities of pollutants reported to be discharged and emitted from wastewater from the 14 existing facilities with Subcategory B and/or D operations only, EPA has determined that the chosen technology basis for the proposed BAT limits is best suited to the type of wastewater the data describe for direct discharges in these subcategories. Technology options 2, 3, and 4, which incorporate steam stripping or steam stripping with distillation technologies, are designed to remove large quantities and many varieties of solvents from process wastewater. They are not optimal treatment technologies for the type of wastestreams reported by the 14 direct dischargers in these subcategories.

The Agency estimated that none of the options would result in any closures or unemployment. Based upon these findings, EPA concluded that all four options are economically achievable. EPA selected Option 1 because it determined that option represented the best available technology from among all the economically achievable options.

In evaluating the non-water quality environmental impacts of the options, specifically electrical power consumption, the Agency found that the annual incremental increase in electrical power consumption for all facilities to achieve Option 1 was 265 megawatts (MW) beyond current usage (the same as for the proposed BPT limits). This is

equivalent to an increase of approximately 0.005 percent of the pharmaceutical industry's purchased electrical energy usage in 1990. The incremental increases for electrical power consumption for the remaining options were: for Options 2 and 3, an increase of 182 MW and 364 MW, respectively, for all facilities for which EPA estimated compliance costs; and for Option 4 an increase of 911 MW for all facilities for which EPA estimated compliance costs.

BAT Options 2, 3, and 4 will generate 76 metric tons per year of condensates as a result of the use of steam stripping or steam stripping with distillation technologies at direct discharging plants. Based on the small increase in condensate generation associated with Options 2, 3, and 4 EPA has concluded that the recovery opportunities or incineration issues prompted by condensate generation do not provide a basis for choosing one of the technology options as the basis for proposed BAT limitations for facilities with Subcategory B and/or D operations. The Agency also considered the effect of these four options on the current levels of air emissions from wastewater at facilities with Subcategory B and/or D operations. To do this, EPA used the WATER7 computer model to evaluate the 1990 levels of air emissions from wastewater for facilities with Subcategory B and/or D operations. The results of the analyses were used to estimate air emission increases or decreases for the regulatory options. The Agency estimates that Option 1 would result in a minimal increase in air emissions, while Options 2, 3, and 4 would decrease air emissions by 16 metric tons per year. EPA concluded that the changes from current emission levels are not significant enough to justify selection of Options 2, 3, and 4.

EPA also concluded that the engineering aspects of all four options were compatible with current manufacturing processes employed and potential process changes at facilities with Subcategory B and/or D operations and thus did not provide a basis for selecting an option. Similarly, the age of equipment and facilities involved did not provide any basis for selecting among the options.

The selection of Option 1 as BAT for facilities with Subcategory B and/or D operations reflects, in large part, EPA's conclusion, based on currently available data, that BPT level biological treatment can degrade the relatively small load of organic pollutants generated by these facilities with a low occurrence of air emissions during advanced biological treatment.

11.4 NSPS

The basis for new source performance standards under Section 306 of the CWA is the best available demonstrated technology. Industry has the opportunity to design and install the best and most efficient pharmaceutical manufacturing processes and wastewater treatment systems at new plants. Accordingly, Congress directed EPA to consider the best demonstrated alternative processes, process changes, in-plant control measures, and end-of-pipe wastewater treatment technologies that reduce pollution to the maximum extent feasible. In response to that directive, and as with the development of options for the proposed BAT effluent limitations guidelines, EPA considered effluent reductions attainable by the most advanced and demonstrated process and treatment technologies at pharmaceutical manufacturing facilities.

The general approach followed by the Agency for developing NSPS options was, where appropriate, to evaluate the best demonstrated processes for control of priority and nonconventional pollutants at the process level and best demonstrated end-of-pipe treatment for control of conventional pollutants and additional control of certain nonconventional pollutants. The factors considered in assessing NSPS include:

- The demonstration status of the process and wastewater treatment technologies;
- The cost of achieving effluent reductions;
- Nonwater quality environmental impacts; and

- Energy requirements.

The NSPS regulatory options considered by the Agency are discussed in Section 7.3.5 and are listed below.

Regulatory Option	Control Technology Description
Subcategories A and C	
NSPS Option 1	In-plant steam stripping with distillation and cyanide destruction, followed by end-of-pipe advanced biological treatment
NSPS Option 2	In-plant steam stripping with distillation and cyanide destruction, followed by end-of-pipe advanced biological treatment and granular activated carbon adsorption
Subcategories B and D	
NSPS Option 1	In-plant steam stripping with distillation followed by end-of-pipe advanced biological treatment
NSPS Option 2	In-plant steam stripping with distillation followed by end-of-pipe advanced biological treatment and granular activated carbon adsorption

11.4.1 Subcategories A and C

EPA selected NSPS Option 1 for Subcategories A and C because EPA has determined that it is the best available demonstrated control technology for treating and removing the pollutants of concern for these subcategories. EPA selected a more stringent NSPS technology than its chosen BAT technology because new sources have the opportunity to segregate their process wastewater in such a way as to minimize the amount of wastewater that will require steam stripping with distillation, thereby reducing the adverse energy impacts that prevented EPA from selecting this technology as BAT.

EPA considered the potential cost of the proposed NSPS technology for new plants, as well as the costs associated with Option 2, which EPA did not select. EPA concluded that costs associated with any option would not be so great as to present a barrier to entry, because EPA anticipated no economic impacts for existing source Subcategory A and C plants if they were to implement the proposed NSPS technology. The Agency also considered energy requirements and other non-water quality environmental impacts when

comparing the GAC technology (Option 2) with Option 1. EPA concluded that there would be only a slight difference in the energy requirements associated with Options 1 and 2. There are no significant differences in the other non-water quality environmental impacts between the two options considered. EPA did not select Option 2 as the proposed basis for NSPS because EPA does not have sufficient data to quantify the amount of COD removed after application of steam stripping with distillation technology and therefore could not determine whether granular activated carbon technology is appropriate to remove remaining COD loads.

The Agency considered energy requirements and other non-water quality environmental impacts and found no basis for any different standards than the proposed NSPS for conventional pollutants.

11.4.2 Subcategories B and D

EPA selected NSPS Option 1 for subcategories B and D. In making this selection, EPA analyzed all of the questionnaire data supplied by facilities with Subcategory B and/or D operations and projected the types and volume of volatile organic pollutants that would be present in treatable levels in process wastewaters from new facilities in these subcategories. Although the Detailed Questionnaire data indicated that process wastewater from the 14 direct dischargers contained fewer pollutants in lower concentrations than the process wastewater of indirect dischargers (therefore justifying proposed effluent limitations based on advanced biological treatment alone, not including steam stripping with distillation), EPA has determined that there is no basis to conclude that data would adequately depict the wastewater characteristics of a new direct discharger. Thus, EPA relied instead on the entire universe of facilities with Subcategory B and/or D operations, irrespective of their direct or indirect discharger status, on the theory that these facilities are more plentiful and hence statistically more significant. Because the EPA has no basis for concluding that the wastewater characteristics are related to the manner of discharge, EPA saw no reason to confine its NSPS analysis to

the 14 existing direct dischargers and to ignore the 67 indirect dischargers that reported data. In evaluating all of the data available to it for these subcategories from the Detailed Questionnaire, EPA concluded that the vast majority of facilities with Subcategory B and/or D operations have process wastewater with a comparatively wide variety of volatile organic pollutants in comparatively high concentrations, as reported by 67 of the 188 existing indirect discharging plants with Subcategory B and/or D operations. EPA considers wastestreams of these 67 plants to be more typical of the wastestreams EPA expects to find in new sources in these subcategories. Therefore, EPA concluded that the process wastewater of new facilities with Subcategory B and/or D operations was more likely to resemble the more typical Subcategory B and/or D wastestreams, not the atypical wastestreams reported by the 14 existing direct dischargers in those subcategories. Based on that conclusion, EPA selected, as the proposed technology basis for NSPS for facilities with Subcategory B and/or D operations, in-plant steam stripping with distillation treatment followed by end-of-pipe advanced biological treatment, which EPA has concluded represents the best available demonstrated treatment technology. EPA selected a more stringent NSPS technology than its chosen BAT technology because new sources have the opportunity to segregate their process wastewater in such a way as to minimize the amount of wastewater that will require steam stripping with distillation, thereby reducing the adverse energy impacts that prevented EPA from selecting this technology as BAT.

EPA considered the potential cost of the proposed NSPS technology for new plants. EPA concluded that costs associated with either option would not be so great as to present a barrier to entry. EPA predicted no economic impacts (i.e., closures) for existing source Subcategory B and D plants if they were to implement the equivalent technology options considered as possible BAT for those subcategories.

The Agency also considered energy requirements and other non-water quality environmental impacts when comparing the GAC technology (Option 2) with Option 1. EPA concluded that there would be only a slight difference in the energy requirements

associated with Options 1 and 2. There are no significant differences in the other non-water quality environmental impacts between the two options considered. EPA did not select Option 2 as the proposed basis for NSPS because EPA does not have sufficient data to quantify the amount of COD removed after application of steam tripping with distillation technology and therefore could not determine whether granular activated carbon technology is appropriate to remove remaining COD loads.

11.5 PSES

Pretreatment standards for existing sources are designed to prevent the discharge of pollutants which pass through, interfere with, or are otherwise incompatible with the operation of POTWs. The CWA requires pretreatment for pollutants that interfere with or pass through POTWs in amounts that would exceed direct discharge effluent limitations or limit POTW sludge management alternatives, including the beneficial use of sludges on agricultural lands. The Agency is also requiring pretreatment for pollutants that pass through POTWs due to the pollutant exhibiting significant volatilization prior to treatment by a POTW. The transfer of a pollutant to another media (air) through volatilization does not constitute treatment. PSES are to be technology-based and analogous to BAT for removal of priority and nonconventional pollutants.

The PSES regulatory options considered by the Agency are discussed in Section 7.3.6 and are listed below.

Regulatory Option	Control Technology Description
Subcategories A and C	
PSES Option 1	In-plant steam stripping and cyanide destruction
PSES Option 2	In-plant steam stripping with distillation and cyanide destruction
PSES Option 3	In-plant steam stripping with distillation and cyanide destruction, followed by end-of-pipe advanced biological treatment
PSES Option 4	In-plant steam stripping with distillation and cyanide destruction, followed by end-of-pipe advanced biological treatment and granular activated carbon adsorption

Regulatory Option	Control Technology Description
Subcategories B and D	
PSES Option 1	In-plant steam stripping
PSES Option 2	In-plant steam stripping with distillation
PSES Option 3	In-plant steam stripping with distillation followed by granular activated carbon adsorption

The Agency is also co-proposing two implementation scenarios for the selected PSES option. Under co-proposal (1), EPA is proposing to regulate all pollutants found to pass-through or interfere with POTWs as described in EPA's POTW pass-through analysis described in Section 17. Under co-proposal (2), EPA is proposing to regulate only highly volatile pollutants at indirect dischargers and is taking comment on the pass-through analysis for other pollutants of concern. See Section 17 for further discussion of the two co-proposals.

11.5.1 Subcategories A and C

EPA selected Option 1 for PSES under both co-proposals for Subcategories A and C. The Agency has evaluated the costs of this option based on co-proposal (1), which is more expansive, and found that there would be no closures among affected facilities (for which costs were estimated by EPA) as a result of these costs. Therefore EPA determined the costs of Option 1 to be economically achievable under either co-proposal. EPA also found the other options to be economically achievable. EPA selected Option 1 because it determined that this option represents the best available technology among all economically achievable options, insofar as it achieves pollutant reductions necessary to prevent pass-through of volatile organic pollutants, allows for recovery and recycling of volatile organic pollutants, and reduces non-water quality environmental impacts caused by air emissions of pollutants from wastewater. The Subcategory A and/or C indirect discharging facilities reported in their questionnaire responses that they emit from wastewater a total of 3,850 million pounds/year of volatile organic pollutants (in contrast to the emissions totaling 3,220 million pounds/year by

direct dischargers). Subsequent analysis using the WATER7 model indicate that these indirect dischargers may actually emit closer to 17,900 million pounds/year from wastewater (in contrast to the emissions totaling 14,000 million pounds/year for the direct dischargers). Although Options 2, 3, and 4 would achieve essentially the same decrease in the emission of wastewater pollutants to the air as Option 1, the increase in energy use requirements associated with Options 2, 3, and 4 would be equivalent to an increase of 31 percent above the 1990 pharmaceutical industry energy use. For this reason, EPA selected Option 1 over Options 2, 3, and 4.

The Agency also considered age, size, processes, other engineering factors, and non-water quality environmental impacts in developing the proposed PSES for Subcategories A and C. The Agency did not identify any basis for establishing different pretreatment standards based on age, size, processes, or other engineering factors.

11.5.2 Subcategories B and D

EPA also selected Option 1 for PSES under both co-proposals for Subcategories B and D. In selecting steam stripping as the technology basis for the proposed PSES for Subcategories B and D, EPA relied upon the 1990 questionnaire data supplied by 188 facilities with Subcategory B and/or D operations that sent their wastewater to POTWs for treatment. The data supplied by the 188 indirect facilities with Subcategory B and D operations, show that these facilities discharge BOD_5, TSS, COD, 18 nonconventional pollutants and four priority pollutants. EPA's analysis of the questionnaire data indicates that the total nonconventional and priority pollutant loadings discharged, on average, for each indirect discharger with Subcategory B and D operations in 1990 was 14,600 pounds/year (in contrast to the average of 1,660 pounds/year reported by the 14 direct dischargers in these subcategories). The 188 facilities also reported in their questionnaire responses that they emit from wastewater a total of 1.5 million pounds/year of volatile organic pollutants (in contrast to the emissions totaling 170 pounds/year reported by the direct dischargers). Subsequent analysis using the

WATER7 model indicates that these indirect dischargers may actually emit closer to 3.3 million pounds/year from wastewater (in contrast to the emissions totaling 35,000 pounds/yr for the direct dischargers). Based on evaluation of this data, EPA selected Option 1 as the basis of pretreatment standards for facilities with Subcategory B and D operations. This technology is designed to remove large quantities and many varieties of solvents from process wastewater. According to the data supplied by the 188 indirect dischargers with Subcategory B and D operations, EPA has concluded that the wastewater characteristic of these facilities--with its comparatively high volume and concentration of solvents--is well-suited to this form of treatment. In addition, EPA found that none of the indirect dischargers with Subcategory B and D operations that would incur costs as a result of the proposed PSES limitations (based on the more expansive co-proposal (1)) would close as a result of this option. Therefore EPA determined that the costs of the pollutant reduction achieved by this option under either co-proposal were economically achievable.

The Agency considered age, size, processes, other engineering factors, and non-water quality environmental impacts in developing the proposed PSES for Subcategories B and D. The Agency did not identify any basis for establishing different pretreatment standards based on age, size, processes, or other engineering factors. EPA has also concluded that Option 1 would significantly decrease air emissions and would be consistent with the Administrator's waste minimization and combustion strategy. EPA did not choose Option 2 because, although this option would result in approximately the same decrease in air emissions as Option 1, it would result in a significant increase in total energy use over that required under Option 1.

11.6 PSNS

Pretreatment standards for new sources are designed to prevent the discharge of pollutants that pass through, interfere with, or are otherwise incompatible with the operation of POTWs. The CWA requires pretreatment for pollutants that pass through

POTWs or limit POTW sludge management alternatives, including the beneficial use of sludges on agricultural lands.

The development of regulatory options for PSNS is analogous to the development of options for NSPS, in that the new source has the opportunity to design and install the best and most efficient pharmaceutical manufacturing processes and wastewater treatment facilities. Accordingly, Congress directed EPA to consider the best demonstrated alternative processes, process changes, in-plant control measures, and end-of-pipe wastewater treatment technologies that reduce pollution to the maximum extent feasible. In response to that directive, EPA considered effluent reductions attainable by the most advanced and demonstrated process and treatment technologies at pharmaceutical manufacturing facilities. The factors considered in assessing PSNS include:

- The demonstration status of the process and wastewater treatment technologies;
- The cost of achieving effluent reductions;
- Nonwater quality environmental impacts; and
- Energy requirements.

The PSNS regulatory options considered by the Agency are discussed in Section 7.3.7 and are listed below.

Regulatory Option	Control Technology Description
Subcategories A and C	
PSNS Option 1	In-plant steam stripping with distillation and cyanide destruction
PSNS Option 2	In-plant steam stripping with distillation and cyanide destruction, followed by end-of-pipe advanced biological treatment
PSNS Option 3	In-plant steam stripping with distillation and cyanide destruction, followed by end-of-pipe advanced biological treatment and granular activated carbon adsorption

Regulatory Option	Control Technology Description
Subcategories B and D	
PSNS Option 1	In-plant steam stripping with distillation
PSNS Option 2	In-plant steam stripping with distillation followed by granular activated carbon adsorption

The Agency is also co-proposing two implementation scenarios for the selected PSNS option. Under co-proposal 1, EPA is proposing to regulate all pollutants found to pass-through or interfere with POTWs as described in EPA's POTW pass-through analysis described in Section 17. Under co-proposal 2, EPA is proposing to regulate only highly volatile pollutants at indirect dischargers and is taking comment on the pass-through analysis for other pollutants of concern. See Section 17 for further discussion of the two co-proposals.

The Agency selected PSNS Option 1 as the basis of NSPS for Subcategory A, B, C, and D operations. Option 1 in all subcategories provides treatment of priority and nonconventional pollutants by in-plant steam stripping with distillation prior to biological treatment, which, for indirect dischargers, occurs at the receiving POTW. EPA also proposes to set standards based on cyanide destruction for cyanide-bearing wastestreams at new source Subcategory A and/or C operations.

EPA selected a more stringent PSNS technology than its chosen PSES technology because new sources have the opportunity to segregate their process wastewater in such a way as to minimize the amount of wastewater that will require steam stripping with distillation, thereby reducing the adverse energy impacts that prevented EPA from selecting this technology as PSES.

EPA considered the cost of the proposed PSNS technologies for new plants based on co-proposal (1), which is more expansive than co-proposal (2). EPA has concluded that such costs are not so great as to present a barrier to entry under either co-proposal, as

demonstrated by the fact that currently operating plants are using these technologies. The Agency also considered energy requirements and other non-water quality environmental impacts when comparing the three PSNS technology options for facilities with Subcategory A and/or C operations and the two PSNS technology options for facilities with Subcategory B and/or D operations. EPA concluded that there would be only a slight difference in the energy requirements associated with Options 1, 2, and 3 for Subcategory A and/or C facilities and with Options 1 and 2 for Subcategory B and/or D facilities. There are no significant differences in the other non-water quality environmental impacts between the options considered.

SECTION 12

NONWATER QUALITY ENVIRONMENTAL IMPACTS

12.1 Introduction

Sections 304(b) and 306 of the CWA require EPA to consider the nonwater quality environmental impacts associated with effluent limitations guidelines and standards. In accordance with these requirements, EPA has considered the potential effect of the proposed regulatory options for the pharmaceutical manufacturing industry on energy consumption, air emissions, and solid waste generation. Sections 12.2, 12.3, and 12.4, respectively, discuss these nonwater quality environmental impacts. EPA has also evaluated the potential effect of process wastewater flow rate on these nonwater quality environmental impacts and a summary of a flow sensitivity analysis is discussed in Section 12.5. The Agency's preliminary development of air emission standards is discussed in Section 12.6.

12.2 Energy Impacts

Energy impacts to the pharmaceutical manufacturing industry from the proposed regulatory options will include increased electrical usage and increased energy usage in the generation of steam for steam stripping with and without distillation. These energy impacts are discussed below in Sections 12.2.1 and 12.2.2.

12.2.1 Electrical Usage

According to the Department of Energy, the pharmaceutical manufacturing industry purchased approximately 5,404 $\times$ 10^6 kWh of electrical energy in 1990, accounting for 0.7% of the total U.S. industrial electrical energy purchase (756,646 $\times$ 10^6 kWh) in 1990.[1] The Agency evaluated the annual incremental increase in electrical power

consumption expected under each regulatory option for direct dischargers. These estimated annual incremental increases (in kWh) are shown below.

	Increase in Electrical Energy Consumption (kWh)	
	Subcategory A and C	**Subcategory B and D**
BAT Option 1	1.38×10^6	0.265×10^6
BAT Option 2	13.2×10^6	0.182×10^6
BAT Option 3	13.6×10^6	0.364×10^6
BAT Option 4	13.6×10^6	0.364×10^6

For Subcategory A and C operations, the Agency is proposing BAT Option 2. This option would increase the electrical power consumption by less than one percent of the total electrical power purchased in 1990 by the pharmaceutical manufacturing industry. For Subcategory B and D operations, the Agency is proposing BAT Option 1. This option would increase the electrical power consumption by less than 0.01 percent of the total electrical power purchased in 1990 by the industry.

12.2.2 Energy Usage in the Generation of Steam

Of greater impact is the energy usage required to generate steam under the regulatory options that include either steam stripping or steam stripping with distillation. Steam stripping and steam stripping with distillation are part of BAT and PSES options considered for Subcategory A and C direct and indirect dischargers and Subcategory B and D direct and indirect dischargers. The Agency evaluated the annual incremental increase in energy usage from steam generation expected under each of these options. These estimated annual incremental increases (in kWh) are shown below.

	Increase in Energy Demand Related to Steam Usage (kWh)			
	Subcategory A and C Direct Dischargers	**Subcategory B and D Direct Dischargers**	**Subcategory A and C Indirect Dischargers**	**Subcategory B and D Indirect Dischargers**
BAT Option 2	720×10^6	1.61×10^6	--	--
BAT Option 3	$2{,}220 \times 10^6$	18.6×10^6	--	--
BAT Option 4	$2{,}220 \times 10^6$	18.6×10^6	--	--
PSES Option 1	--	--	749×10^6	90.2×10^6
PSES Option 2	--	--	$2{,}760 \times 10^6$	266×10^6
PSES Option 3	--	--	$2{,}760 \times 10^6$	266×10^6
PSES Option 4	--	--	$2{,}760 \times 10^6$	

According to the Department of Energy (1), the pharmaceutical manufacturing industry purchased approximately $8{,}981 \times 10^6$ kWh of fuel and electric energy in 1990. for Subcategory A and/or C operations at direct dischargers, the Agency is proposing BAT Option 2, which would increase the energy consumption for steam generation by an amount equal to 8 percent of the total fuel and electrical power purchased in 1990. The Agency is not proposing a BAT option that includes steam stripping for Subcategory B and/or D operations at direct dischargers. For Subcategory A and/or C operations at indirect dischargers, the Agency is proposing PSES Option 1 which would increase the energy consumption for steam generation by an amount equal to 8 percent of the total fuel and electrical power purchased in 1990. For Subcategory B and/or D operations at indirect dischargers, the Agency is proposing PSES Option 1, which would increase the energy consumption for steam generation by an amount equal to one percent of the total fuel and electrical power purchased in 1990.

It should be noted, however, that in estimating the energy consumption for steam generation associated with the steam stripping and steam stripping with distillation options, EPA assumed that very high volumes of wastewater would need to be stripped and/or distilled. This assumption was based on the available detailed questionnaire data and leads to the high requirements for steam. EPA believes that this assumption is very conservative, because the Agency assumed from the Detailed Questionnaire responses

that wastewater streams containing high concentrations of volatile organic pollutants could not be segregated from streams containing minimal or no concentrations of these pollutants. EPA believes that stream segregation is possible and that the volume of wastewater that would be subject to steam stripping and distillation is substantially lower than the volume assumed for these energy use calculations. To assess what impact a lower wastewater volume treated would have on steam generation requirements, EPA conducted a flow sensitivity analysis as described in Section 12.5.

Table 12-1 summarizes the estimated increase in energy usage (including electrical power and steam generation) associated with the proposed regulations. Compliance with the proposed regulations is estimated to increase the industry's energy usage by approximately 17.5 percent. While the steam generation required under the proposed regulations requires increased energy consumption, the Agency notes that the potential for solvent recovery and reuse will help to offset these energy expenditures. In addition, these estimates are based on steam stripping of 80 to 100 percent of each facility's process wastewater which the Agency believes could significantly over estimate the steam generation requirements. The Agency concludes that the effluent reduction benefits from the proposed regulation exceed the potential adverse impacts from the increase in energy consumption that is projected.

12.3 Air Emission Impacts

Pharmaceutical manufacturing facilities generate wastewaters that contain varying concentrations of organic compounds, some of which are listed as Hazardous Air Pollutants (HAPs) in Title 3 of the Clean Air Act Amendments (CAAA) of 1990. Table 12-2 lists the HAPs and volatile organic pollutants present in pharmaceutical manufacturing wastewaters, as reported by facilities responding to the Detailed Questionnaire (volatile organic pollutants were identified as those constituents that could be analyzed by standard EPA methods for volatile organics such as gas chromatography mass spectrometry (GCMS) by analytical method 1624 (40 CFR Part 136) or GC by

analytical method 8015.[2]). Prior to discharge, pharmaceutical manufacturing wastewaters typically pass through a series of collection and treatment units that are open to the atmosphere. Atmospheric exposure of organic-containing wastewaters can result in significant volatilization of HAPs, volatile organic pollutants, and other organic pollutants to the air.

Air emissions of HAPs, volatile organic pollutants, and other organic pollutants may occur from wastewater collection units such as process drains, manholes, trenches, sumps, and junction boxes, and from wastewater treatment units such as neutralization and equalization basins, settling basins, clarifiers, biological treatment units, air and steam strippers lacking air pollution control devices, and other units that expose wastewater to the air.

To determine the impact of the proposed regulation on air emissions, the Agency had to first determine the current amount of organic constituents emitted into the air from pharmaceutical manufacturing wastewaters. Section 12.3.1 compares the air emissions estimated by facilities responding to the Detailed Questionnaire with the air emissions estimated by a WATER7 model analysis, an independent fate analysis performed by the Agency. Section 12.3.2 discusses the regulatory impact on air emissions based on a comparison of current air emissions from pharmaceutical manufacturing wastewaters to projected air emissions from pharmaceutical manufacturing wastewaters of facilities complying with the proposed regulation.

This section also discusses the estimated impact on criteria pollutant emissions in the generation of steam for regulatory options which include steam stripping and distillation.

12.3.1 Current Air Emissions Based on Detailed Questionnaire Responses and WATER7 Analysis

In response to Section 3a of the Detailed Questionnaire, entitled "Compound or Chemical Usage and Disposition," facilities estimated the quantities of virgin chemicals used and disposed of during manufacturing of pharmaceutical products in calendar year 1990. As part of the chemical usage and disposition reporting, facilities were asked to estimate the amount of virgin chemicals used in pharmaceutical manufacturing operations that was: 1) emitted into the air from wastewater prior to discharge, 2) degraded and/or destroyed, and 3) discharged to a surface water and/or a POTW. These three disposition methods summarize the fate, or disposal pathways, of organic constituents present in pharmaceutical manufacturing wastewaters.

Upon examining responses to the Detailed Questionnaire regarding the fate of wastewater organic constituents, the Agency suspected that a greater percentage of wastewater organic constituents are emitted to the air than most facilities reported. The Agency noted that 20 indirect dischargers that had no on-site wastewater treatment systems reported a large percentage of wastewater organic constituents degraded and/or destroyed on site. It is improbable that such high rates of degradation and/or destruction could be achieved in the absence of any wastewater treatment system, such as biological treatment or incineration. In addition, some plants with open impoundments or basins with mechanical agitators or aerators, reported relatively small percentages of air emissions from wastewater in Table 3-2 of the Detailed Questionnaire. The responses to the detailed questionnaire also lacked in most cases an indication of the estimation method used in determining the load discharged as air emissions from wastewater.

To provide an independent estimate of the partitioning of wastewater organic constituents (including the HAPs and volatile organic pollutants listed in Table 12-2), the Agency performed a fate analysis using the WATER7 model and data provided by the

244 pharmaceutical manufacturing facilities that responded to the Detailed Questionnaire. Facilities were grouped by manufacturing process (Subcategory A and C or Subcategory B and D) and by type of wastewater discharge (direct or indirect). For each facility group, the WATER7 model was used to estimate the amount of reported wastewater organic constituents: 1) emitted to the air from wastewater during collection and treatment, 2) degraded and/or destroyed, or 3) discharged to surface water and/or POTW. In addition, the WATER7 model estimated the amount of reported wastewater organic constituents disposed of as a result of sludge adsorption. The Detailed Questionnaire did not have a separate category for sludge adsorption with regard to organic constituent disposal pathways. Therefore, the responses from facilities did not differentiate the amount of wastewater organic constituents disposed of as a result of sludge adsorption from the amount emitted into the air, degraded and/or destroyed, or discharged to surface water and/or POTW. The amount of wastewater organic constituents disposed of as a result of sludge adsorption was most likely reported by facilities under the degraded and/or destroyed disposal category because wastewater sludge generated is typically incinerated.

The WATER7 model uses the chemical properties data from CHEMDAT7, a database described in the Air Emission Models Report.[3] The model determines wastewater pollutant disposal pathways from the following wastewater treatment units:

- Pretreatment;
- Primary filter;
- Trickling filter;
- Equalization;
- Aeration 1;
- Aeration 2; and
- Secondary clarifier.

The wastewater treatment trains used in the WATER7 model to simulate the wastewater treatment trains of the facilities responding to the Detailed Questionnaire consisted of a combination of the various treatment units listed above. The wastewater pollutant data

and pollutant loading data used as input for WATER7 model analysis were compiled from facility responses to Section 3a of the Detailed Questionnaire. Information on treatment unit characteristics used as input for WATER7 model analysis were compiled from facility responses to Section 5 of the Detailed Questionnaire. A complete description of the WATER7 model, the fate analysis, and the assumptions made for the fate analysis is presented in the May 18, 1994 memorandum entitled WATER7 Analysis of the Fate of Organic Pollutant Loads through Pharmaceutical Facilities [4], located in the Record for this rulemaking.

Table 12-3 presents the results of the WATER7 analysis for direct dischargers, listed by subcategory, and the corresponding estimates reported by direct dischargers responding to the Detailed Questionnaire. Table 12-4 presents the results of the WATER7 analysis for indirect dischargers and the corresponding estimates reported by indirect dischargers responding to the Detailed Questionnaire. For both direct and indirect dischargers, the results of the WATER7 analysis indicate that a significantly higher percentage of wastewater organic constituents partition to the air than was reported by facilities responding to the Detailed Questionnaire. For example, Subcategory A and C indirect dischargers estimated that approximately 90.5 million pounds of constituents present in pharmaceutical manufacturing wastewaters in 1990 were: 1) emitted into the air from wastewater, 2) degraded and/or destroyed, or 3) discharged to POTWs. Of this total, the Subcategory A and C indirect dischargers reported that approximately 4% was emitted into the air, 59% was degraded and/or destroyed, and 37% was discharged to POTWs. In comparison, of the 90.5 million pounds of wastewater constituents reported by facilities, the WATER7 model analysis estimated that 20% would be emitted into the air, 36% would be degraded and/or destroyed, 43% would be discharged to POTWs, and 1% would be disposed of by sludge adsorption.

Overall, a total of 8.5 million pounds of organic pollutants were reported as emitted into the air in 1990 from pharmaceutical manufacturing wastewaters based on summarized Detailed Questionnaire responses. The WATER7 model estimated that approximately

35.2 million pounds of organic pollutants were emitted into the air in 1990 from pharmaceutical manufacturing wastewaters, four times the estimate reported by facilities in the Detailed Questionnaire.

12.3.2 Regulatory Impact on Air Emissions

The use of in-plant steam stripping as part of the Agency's proposed regulatory options will impact air emissions in two ways. First, priority and nonconventional pollutants that are currently released as air emissions from wastewater at pharmaceutical manufacturing facilities will be removed and condensed by in-plant steam stripping for recycle, reuse, or disposal. Second, the generation of steam for steam stripping or steam stripping with distillation options will result in increased emissions of criteria pollutants (CO, NO_x, VOC, SO_2, and particulate matter). EPA's evaluation of these impacts are described in Sections 12.3.2.1 and 12.3.2.2 below.

12.3.2.1 Reduction in Air Emissions Due to Proposed Regulatory Options

As discussed in Section 11, the Agency is proposing effluent limitations guidelines and standards for ammonia and organic pollutants based on the following in-plant and end-of-pipe treatment technologies:

Subcategory	Discharge Status	Proposed BAT/PSES Treatment Technologies for Organic Pollutants
A and C	Direct	In-plant steam stripping followed by end-of-pipe advanced biological treatment
A and C	Indirect	In-plant steam stripping
B and D	Direct	End-of-pipe advanced biological treatment
B and D	Indirect	In-plant steam stripping

The Agency estimates that the proposed BAT and PSES options that include in-plant steam stripping will remove organic pollutants and ammonia currently discharged as air emissions from wastewater as follows:

Regulatory Option	Subcategory	Estimated Reduction in Air Emissions (lbs/yr)
BAT Option 2	A and C	13.5×10^6
BAT Option 1	B and D	(a)
PSES Option 1	A and C	17.9×10^6 (b)
PSES Option 1	B and D	3.08×10^6 (b)

(a) The Agency expects that application of advanced biological treatment for Subcategory B and D direct dischargers will result in a minimal increase in air emissions of organic pollutants from wastewater due to the addition of open aeration under this option.
(b) These reductions assume implementation of PSES co-proposal (1).

These reductions should occur since the proposed technology basis of in-plant steam stripping is applied at a point prior to dilution of process wastewaters and prior to exposure of the wastestreams to the air.

12.3.2.2 Criteria Pollutant Air Emissions

EPA evaluated the impact of steam generation requirements, under regulatory options that include in-plant steam stripping and steam stripping with distillation, on criteria pollutant emissions. To develop this estimate, the total steam generation requirements in tons of steam were estimated using the pharmaceutical cost model and it was assumed that the steam would be generated in industrial boilers with no emission controls. Fifty percent of the required boiler fuel is assumed to be low sulfur Number 6 fuel oil and the remaining 50% supplied by natural gas. The calculation of criteria pollutant air emissions is presented in the December 15, 1994 calculation package entitled Calculation of Air Emissions Related to Steam Generation.[5] Table 12-5 presents an estimate of the resultant criteria pollutant emissions.

For those options proposed as the basis of regulation, the resultant criteria pollutant emission total is 3,014 tons/yr or 6.03×10^6 lbs/yr. The Agency concludes that the air emission and effluent reduction benefits of hazardous air pollutants, priority, nonconventional, and conventional pollutants far outweigh the potential negative impacts of increased emissions of criteria air pollutants.

12.4 Solid Waste Impacts

The Agency has evaluated the following solid waste impacts which would be expected due to the application of the proposed BPT, BCT, BAT, and PSES effluent limitations guidelines and standards:

- The increase in dry sludge generation due to the application of advanced biological treatment;
- The increase in waste solvent generation due to the application of in-plant steam stripping and in-plant steam stripping with distillation; and
- The increase in waste hydrogen chloride (HCl) due to scrubber liquor generated by facilities with wastewaters containing ammonia.

These impacts are discussed below in Sections 12.4.1, 12.4.2, and 12.4.4, respectively. Section 12.4.3 presents an overview of EPA's waste minimization and combustion strategy including EPA's approach for clean fuels. The Agency is not proposing any BAT or PSES options which include activated carbon treatment and therefore there are no solid waste impacts associated with this technology.

12.4.1 Dry Sludge Generation

Based on the responses to the Detailed Questionnaire, pharmaceutical manufacturers generated approximately 112,000 tons of dry sludge in 1990. Table 12-6 presents the

amount of sludge (dry basis) generated in 1990 by Subcategory A and/or C and Subcategory B and/or D direct and indirect dischargers as well as the estimated amount of additional dry sludge that would be generated by Subcategory A and/or C and Subcategory B and/or D direct and indirect dischargers facilities complying with the proposed effluent limitations guidelines.

Compliance with BAT/BPT/BCT is expected to increase the mass of wastewater treatment sludge generated by Subcategory A and/or C direct dischargers by 5,180 tons/yr, a result of increased solids generation and removal at facilities upgrading to advanced biological treatment systems. This represents approximately a 14% increase in the current sludge generation rate of 36,400 tons/yr for Subcategory A and/or C direct dischargers.

Compliance with BAT/BPT/BCT is expected to increase the mass of wastewater treatment sludge generated by Subcategory B and/or D direct dischargers by 44 tons/yr, a result of increased solids generation and removal at facilities upgrading to advanced biological treatment systems. This represents less than a 2% increase in the current sludge generation rate of 2,760 tons/yr for Subcategory B and/or D direct dischargers.

Compliance with BAT/BPT/BCT is anticipated to improve the quality of wastewater treatment sludge by reducing mass loadings of pollutants exported in sludge. The Agency concludes that there will be no adverse non-water quality environment impacts regarding sludge management.

No additional sludge is expected to be generated by facilities that discharge directly as a result of the proposed regulations.

12.4.2 Waste Solvent Generation

Compliance with BAT for Subcategory A and/or C direct dischargers and compliance with PSES for Subcategory A and/or C and Subcategory B and/or D indirect dischargers is expected to increase the amount of waste solvents generated by pharmaceutical manufacturing facilities as a result of in-plant steam stripping. The amount of waste solvents recovered as a result of steam stripping by Subcategory A and/or C direct dischargers would be approximately 57,300 tons/yr or 52,000 metric tons/yr. The amount of waste solvents recovered as a result of steam stripping by Subcategory A and/or C and Subcategory B and/or D indirect dischargers would be approximately 63,500 and 6,370 tons/yr, respectively or 57,600 and 5,780 metric tons/yr, respectively. As discussed previously, the use of in-plant steam stripping would remove a significant amount of organic pollutants from the wastewater prior to atmospheric exposure of the wastewater and the subsequent emission of pollutants into the air.

Organic solvent overheads generated under the proposed BAT and PSES options will create the opportunity for additional solvent recovery or reuse in the pharmaceutical manufacturing industry. For example, the Agency is aware of at least one pharmaceutical manufacturer that is currently distilling methanol from a process wastewater stream and recycling the concentrated methanol overheads back into their process operation. The Agency is also aware of at least two other pharmaceutical manufacturers that steam strip their process wastewaters and sell the solvent overheads for profit. Where possible, facilities would be expected to recover solvents for reuse within the process or for use in other industrial processes.

The solvent overheads will also have a value associated with their energy content. The Agency has estimated that the energy value of the solvent overheads generated under the proposed options will be 77.4 million kWhr/yr for Subcategory A and/or C direct dischargers. The energy value of the solvent overheads generated by

Subcategory A and/or C and B and/or D indirect discharging facilities is estimated as 85.7 and 8.6 million kWhr/yr, respectively.

12.4.3 Waste Minimization and Combustion Strategy

In May 1994, the EPA Administrator announced a Draft Hazardous Waste Minimization and Combustion Strategy that is pertinent to the pharmaceutical manufacturing industry. The Draft Strategy provides the central framework for EPA's federal effort to maximize the source reduction and recycling of hazardous wastes under RCRA. The Draft Strategy focuses on a number of specific goals, including reducing the amount and toxicity of hazardous waste that is generated, particularly when such reductions would benefit more than one environmental medium. The Draft Strategy also encompasses a number of other features, including public outreach, public involvement and environmental justice, permitting, enforcement, risk assessments, and good science.[6]

12.4.3.1 Waste Minimization

The Draft Strategy has both short-term and a longer-term phases. In the short-term, EPA will address the source reduction and environmentally sound recycling of halogenated (and metal-bearing) combustible wastes. The longer-term effort will encompass all RCRA hazardous wastes, taking a more comprehensive approach to how wastes are generated and managed, and the role waste minimization can play as a preferred "mode of management" over other forms of waste management (e.g., treatment, storage, and disposal). This source reduction (waste minimization) strategy should reduce the long-term demand for combustion and other waste management facilities.(6) Section 7.2 presents EPA's efforts toward increasing opportunities for source reduction (e.g., process changes) in the pharmaceutical manufacturing industry.

The Agency also has released a draft report by the EPA Office of Solid Waste's Definition of Solid Waste Task Force. This report, Reengineering RCRA for

Recycling [7], presents recommendations of the Task Force to improve the regulation of hazardous waste recycling under RCRA. One of the recommendations of the Task Force was that provision should be made to exempt "clean" waste-derived fuels from the regulatory requirements of RCRA for hazardous wastes. "Clean fuels" are fuels with "*de minimis*" levels of halogens (primarily chlorine in this case) or toxic metals, especially fuels that are characteristically hazardous only because of ignitability. EPA will address the recommendations of the Task Force, including the recommendation on "clean fuels."

In the case of the pharmaceutical manufacturing industry, the volatile organic pollutants that are generated in the largest quantities are non-halogenated volatile organic pollutants, including methanol, ethanol, isopropanol, and acetone. Implementation of in-plant steam stripping technology affords the opportunity to recover these pollutants and reuse them for their solvent properties. In situations where reuse of solvents is not practical, these non-halogenated pollutants can potentially be used as "clean fuels" in industrial boilers, such as those on-site at pharmaceutical manufacturing facilities.

Implementation of in-plant steam stripping also affords the opportunity to recover halogenated volatile organic pollutants (e.g., methylene chloride) for recycle in the pharmaceutical manufacturing process. Recovered chlorinated solvents that are not of sufficient quality for reuse in pharmaceutical manufacturing processes may be sold for reuse in other industries.

12.4.3.2 Combustion

The Draft Strategy also addresses rigorous controls on hazardous waste combustion facilities using best available technologies to ensure that these facilities do not impose unacceptable risk to human health and the environment. EPA's regulatory activities are scheduled to be directed toward upgrading technical standards for residual wastes and emissions from hazardous waste combustion facilities, including incinerators, cement

kilns, light-weight aggregate kilns, and smelter furnaces, as well as boilers and industrial furnaces.

EPA estimates that approximately 127,000 tons per year or 115,000 metric tons per year of solvent waste (halogenated and nonhalogenated) would be recovered from in-plant steam stripping at pharmaceutical manufacturing facilities. Currently there is RCRA-permitted capacity at commercially available facilities to incinerate in excess of 1 million metric tons per year of solvents. Therefore, there is adequate capacity at commercial incinerators to combust the entire mass of solvents assuming that none would be recovered and recycled. Again, however, it is the Agency's policy, as stated in the Draft Waste Minimization and Combustion Strategy, that the most appropriate mode of management for solvents removed from pharmaceutical manufacturing wastewaters by steam stripping is recycle in the process, recycle at other facilities, or use as "clean fuels" in boilers.

12.4.4 Waste Hydrogen Chloride Scrubber Liquor

Compliance with BAT for Subcategory A and/or C direct dischargers and compliance with PSES for Subcategory A and/or C indirect dischargers is expected to increase the amount of waste hydrogen chloride (HCl) scrubber liquor recovered by pharmaceutical manufacturing facilities that generate wastewaters containing ammonia. HCl wet scrubbers are used to control air emissions from steam strippers used to remove ammonia from the wastewater. The amount of waste scrubber liquor generated by Subcategory A and/or C direct dischargers would be approximately 467 tons/yr. The amount of waste scrubber liquor generated by Subcategory A and/or C indirect dischargers would be approximately 706 tons/yr.

12.5 Flow Sensitivity

To evaluate the impact of process wastewater flow on nonwater quality environmental impacts, EPA evaluated the impact on electricity and steam usage assuming a facility's process wastewater organic load is contained in a smaller volume of flow. Table 12-7 presents a summary of the flow sensitivity analysis conducted for Subcategory A and/or C direct dischargers under BAT Option 3 (in-plant steam stripping with distillation followed by end-of-pipe advanced biological treatment) and Subcategory A and/or C and B and/or D indirect dischargers under PSES Option 2 (In-plant steam stripping with distillation). Under this analysis, all process wastewater is treated through end-of-pipe biological treatment (for direct dischargers) but the organic load is assumed to be concentrated in a portion of the process wastewater flow for the in-plant steam stripping with distillation treatment. The flow sensitivity analysis shows that segregation of high concentration wastewaters from dilute process wastewaters could significantly reduce the steam generation required under the proposed regulatory options which include in-plant steam stripping with distillation and in-plant steam stripping.

12.6 Preliminary Development of Air Emission Standards

Title III of the 1990 Clean Air Act Amendments was enacted to reduce the amount of nationwide emissions of hazardous air pollutants. It comprehensively amended section 112 of the Clean Air Act (CAA).

Section 112(b) lists the 189 chemicals, compounds, or groups of chemicals deemed by Congress to be hazardous air pollutants (HAPs). These toxic air pollutants are to be regulated by national emission standards for hazardous air pollutants (NESHAP). Section 112(c) requires the Administrator to use this list of HAPs to develop and publish a list of source categories for which NESHAP will be developed. EPA must list all known categories and subcategories of "major sources."

The term major source is defined in paragraph 112(a)(1) to mean any stationary source or group of stationary sources located within a contiguous area and under common control that emits or has the potential to emit, considering controls, in the aggregate 10 tons per year (tons/yr) or more of any HAP or 25 tons/yr or more of any combination of HAPs. The term stationary source, from section 111 of the CAA, means any building, structure, facility, or installation that emits or may emit any air pollutant. The term area source, as defined in section 112(a)(2), means any stationary source of HAPs that is not a major source.

Notice of the initial list of categories of major and area sources of HAPs was published on July 16, 1992 (57 FR 31576), under authority of section 112(c). This notice listed pharmaceutical manufacturing as a category of major sources of HAPs. Notice of the schedule for the promulgation of emission standards for the listed categories, under authority of section 112(e), was given on December 3, 1993 (58 FR 63941). Under this notice, emission standards for the pharmaceutical production industry would be promulgated no later than November 15, 1997.

Section 112(d) of the CAA directs the Administrator to promulgate emission standards for each category of HAP sources listed under section 112(c). Such standards are applicable to both new and existing sources and must require the maximum degree of reduction in emissions of the hazardous air pollutants subject to this section (including a prohibition on such emissions, where achievable) that the Administrator, taking into consideration the cost of achieving such emission reduction, and any non-air quality health and environmental impacts and energy requirements, determines is achievable for new and existing sources in the category or subcategory to which such emission standard applies. See 42 U.S.C. 7412(d)(2).

Section 112(d)(3) provides that the maximum degree of reduction in emissions that is deemed achievable for new sources shall not be any less stringent than the emission control that is achieved in practice by the best controlled similar source. For existing

sources, the standards may not be less stringent than the average emission limitation achieved by the best performing 12 percent of existing sources in each category of 30 or more sources.

Once this minimum control level (referred to as the floor) has been determined for new or existing sources for a category, the Administrator must set a standard based on maximum achievable control technology (MACT) that is no less stringent than the floor. The Administrator may set MACT standards that are more stringent that the floor if such standards are achievable considering the cost, environmental, and other impacts listed in section 112(d)(2). Such standards must then be met by all sources within the category.

EPA is in the early stages of developing the MACT standard for pharmaceutical facilities; the standards will require the control of several different emission points, including organic air emissions from wastewater operations. EPA recently promulgated a similar MACT standard for organic HAP emissions from the Synthetic Organic Chemical Manufacturing Industry (SOCMI). This rule, often referred to as the Hazardous Organic NESHAP or HON, was published on April 22, 1994 (59 FR 19402). On January 7, 1993, EPA published amendments to the Benzene Waste Operations NESHAP, which controls benzene emissions from wastewater operations based upon Clean Air Act authority predating the 1990 amendments (40 CFR Part 61 Subpart FF).

The control approach that EPA is considering for the pharmaceutical manufacturing industry is similar to the approach EPA used in the SOCMI HON and the Benzene Waste Operations NESHAP to control organic air emissions from wastewater collection and treatment operations. That approach consists first of identifying a subset of wastewater streams that require control through a combination of wastewater flow rate and concentration action levels, and second, the control requirements for these affected streams. The flow rate and concentration of each wastewater stream would be

determined to reflect the characteristics at the point of generation of the wastewater stream.

The point of generation is defined to be where each individual wastewater stream exits production process equipment prior to any form of wastewater treatment. The characteristics of a wastewater stream at the point of generation are used to determine which streams to control because this is where the organic concentration is the highest and the flow is the lowest. The use of the point of generation characteristics in this way results in the identification of the most cost effective streams for control. If the characteristics of the streams were determined at some point downstream of the point of generation, there would be losses of organics due to air emissions and an increase in the wastewater flow rate due to mixing with other wastewater streams, both of which would result in the subsequent control of the stream being less cost effective. In addition, if wastewater treatment were allowed before the point of generation, the treatment unit, such as an air stripper, would not be required to have air emission control.

The flow rate action level is generally expressed as the liters per minute of wastewater flow. Values of flow rate used in previous regulatory analyses range from 0.02 to 10 liters per minute.

The concentration action level is based on the "volatile organic" concentration of the wastewater stream rather than the total concentration. EPA has developed a test method, Method 305 in Appendix A of 40 CFR Part 63, to determine the volatile organic HAP concentration for use with wastewater MACT standards. The purpose of this test method is to determine a relative measure of the emission potential of a typically controlled wastewater stream by measuring essentially all of an organic HAP compound that is likely to be emitted in significant quantities while measuring essentially none of an organic HAP compound that is unlikely to be emitted. Previous regulatory analyses have used an action level of 10,000 ppmw at any flow rate and coupled with a

range of action levels from 10 to 1,000 ppmw tied to a flow rate cutoff as described above.

Examples of the use of these action levels in recent rules include the Benzene Waste Operations NESHAP, which has action levels of 0.02 liters per minute and 10 ppmw benzene, and the HON, which has a 10,000 ppmw volatile organic HAP concentration action level at any flow rate coupled with an action level pair of 10 liters per minute and 1,000 ppmw volatile organic HAP concentration.

The control requirements for affected wastewater streams include managing the identified wastewater streams in controlled units during collection and treatment to remove or destroy the organics. This control approach includes: 1) suppression or control of air emissions from the point of wastewater generation to the treatment device by installing controls on the sewer system, tanks, and containers used to transport the wastewater; 2) treatment of the wastewater to remove or destroy the organics; 3) control of air emissions from the treatment device (e.g., the non-condensible air emissions from the stripper condenser); and 4) control or recycling of the organics removed by the treatment device (e.g., the condensed residuals collected by the stripper condenser).

The treatment device used as the basis for the HON is a steam stripper, the same device proposed as the primary technology basis for the proposed pharmaceutical industry limitations and standards. The HON requirements are performance standards, so that any device that achieves the desired performance can be used. In addition, the HON allows several compliance alternatives including the use of open biological treatment units to treat the wastewater if a controlled collection and treatment system is used up to the unit and the unit can be demonstrated to achieve the required level of biological degradation. The HON requires the use of the procedures outlined in Appendix C of 40 CFR Part 63 to demonstrate that the organics are being degraded by the biological treatment unit and not emitted to the air.

The CAAA also requires EPA to establish Control Techniques Guideline (CTG) documents for the states to use to develop volatile organic pollutant emissions control plans for ozone nonattainment areas. Industrial wastewater, which includes the pharmaceutical manufacturing industry, is one of the source categories for which EPA is developing a CTG document (see the draft document entitled "Control of Volatile Organic Compound Emissions from Industrial Wastewater," EPA-453/D-92-056, September 1992; available in the record). Based on this guidance, certain states will write rules for volatile organic pollutant emissions from wastewater operations at pharmaceutical facilities located in ozone nonattainment areas. These rules are expected to be similar to the MACT standards, except they would control additional wastewater streams based on their potential for volatile organic pollutant emissions rather than HAP emissions. The concentration action level used in the draft CTG is based on the volatile organic concentration, which is determined by Method 25D in Appendix A of 40 CFR part 60.

The volatile organic HAP and flow rate action levels for the MACT standard for pharmaceutical plants have not yet been determined. EPA has conducted a preliminary analysis of the impacts of a set of control options (action levels) for direct and indirect dischargers of Subcategory A and C, and Subcategory B and D based on the approaches used in the HON. EPA emphasizes that this analysis is still preliminary. Wastewater data from the Detailed Questionnaire responses were used in the analysis; however, a number of assumptions were made. See the draft document entitled "Control of Volatile Organic Compound Emissions from Industrial Wastewater," EPA-453/D-92-056, September 1992, for presentation of the assumptions and methodology used for this preliminary analysis. During the development of the MACT standard, this analysis will be refined based on new information and comments from the public.

Tables 12-8 and 12-9 summarize the results of this preliminary analysis. Two sets of preliminary results are presented based on two ways to evaluate the existing data for effluent guideline Subcategory A, B, C, and D facilities. The actual results of a rule

based on any of the control options could be very different than these preliminary impacts. Table 12-8 presents results based on applying the controls described above to wastewater streams that are equal to or greater than the identified action levels as the streams were reported in the Detailed Questionnaire responses. This database reflects the characteristics of combined process area wastewater streams, not the point of generation of the wastewater. Table 12-9 presents results based on the same criteria, but the Detailed Questionnaire wastewater data have been disaggregated in an attempt to simulate the characteristics at the point of generation. This disaggregation was performed in the manner described in Appendix B of the draft CTG document.

The control options (action levels), which encompass different combinations of volatile organic HAP (VOHAP) and wastewater stream flow rates, identified in both tables are ones that were considered in the development of the HON. All of the control options would require control of any wastewater stream that has 10,000 ppmw or greater volatile organic HAP concentration. The least stringent control option identified would require all wastewater streams with a flow of 10 liters per minute or greater and a 1,000 ppmw or greater volatile organic HAP concentration be equipped with controls. Wastewater streams below these criteria would not require control. Other more stringent control options would have lower action levels and require more wastewater streams to be controlled. The most stringent control option shown would require all streams with a flow of 1.0 liters per minute or greater and a 100 ppmw or greater volatile organic HAP concentration be controlled.

The analysis will be refined, and these results, along with other statutory criteria in the Clean Air Act, will be considered before a MACT standard for the pharmaceutical manufacturing industry is proposed.

It is the Agency's intent for both the effluent guidelines proposed in this document and the MACT standards to be proposed at a later date that upon promulgation the in-plant technology basis of both rules will be applicable to essentially the same high

concentration low volume process wastewater streams in which the bulk of the volatile organic pollutants are contained, as represented preliminarily by Tables 12-8 and 12-9. The practical effect of this approach will be that only a relatively small portion (i.e., substantially less than half) of all process wastewaters will require control by a treatment device (e.g., steam stripping) to achieve both rules. EPA has been informed by the industry that additional data will be submitted (some data have been submitted) in order to characterize, in greater detail than available in responses to the Detailed Questionnaire, the individual process wastewater streams at the point of generation. This additional data and any other information available to EPA will be considered prior to promulgation in identifying the small portion of process wastewater streams that would require control of volatile organic pollutants under both the effluent limitations guidelines and the MACT standard for this industry.

Table 12-1

Regulatory Impact on Energy Usage

Facility Subcategories	Regulation	Source of Increased Energy Usage	Amount of Increase in Energy Usage (1×10^6 kWh)
Subcategory A and C Direct Dischargers	BPT/BAT	In-plant Steam Stripping + Steam Usage + Cyanide Destruction Pretreatment + Advanced Biological Treatment	733
Subcategory B and D Direct Dischargers	BPT/BAT	Advanced Biological Treatment	0.265
Subcategory A and C Indirect Dischargers	PSES	In-plant Steam Stripping + Steam Usage	752
Subcategory B and D Indirect Dischargers	PSES	In-plant Steam Stripping + Steam Usage	90.8
		Total	1,576

Table 12-2

HAPs and Volatile Organic Pollutants Present in Pharmaceutical Manufacturing Wastewaters

HAPs		Volatile Organic Pollutants	
Const. Code	**Chemical Name**	**Const. Code**	**Chemical Name**
3	Acetonitrile	3	Acetonitrile
12	Aniline	10	n-Amyl acetate
15	Benzene	11	Amyl alcohol
22	Bis(chloromethyl)ether	15	Benzene
25	2-Butanone (MEK)	25	2-Butanone (MEK)
35	Chlorobenzene	26	n-Butyl acetate
37	Chloroform	27	n-Butyl alcohol
39	Chloromethane	29	tert-Butyl alcohol
62	N,N-Dimethylaniline	35	Chlorobenzene
64	N,N-Dimethylformamide	37	Chloroform
67	1,4-Dioxane	39	Chloromethane
77	Ethylene glycol	43	Cyclohexane
79	Formaldehyde	51	1,2-Dichloroethane
83	Glycol ethers	58	Diethyl ether
87	n-Hexane	66	Dimethyl sulfoxide
97	Methanol (Methyl alcohol)	67	1,4-Dioxane
102	Methylene chloride	70	Ethanol
105	Methyl isobutyl ketone (MIBK)	71	Ethyl acetate
114	Phenol	77	Ethylene glycol
130	Toluene	84	n-Heptane
136	Triethylamine	87	n-Hexane
139	Xylenes	94	Isopropanol
		97	Methanol
		101	Methyl cellosolve
		102	Methylene chloride
		103	Methyl formate
		105	Methyl isobutyl ketone (MIBK)
		117	n-Propanol
		118	Acetone
		130	Toluene
		134	Trichlorofluoromethane
		139	Xylenes

Table 12-3

Estimates of Disposal Partitioning for Organic Constituents Released to Wastewater for Direct Dischargers

Disposal Pathway of Organic Constituents Released to Wastewater (WW)	Subcategory A and C Direct Dischargers				Subcategory B and D Direct Dischargers			
	Detailed Questionnaire Response		WATER7 Results		Detailed Questionnaire Response		WATER7 Results	
	1,000 lbs / yr	% of Total Released	1,000 lbs / yr	% of Total Released	1,000 lbs / yr	% of Total Released	1,000 lbs / yr	% of Total Released
Emitted into air from WW	3,220	4.2	14,000	18.1	0.17	0.1	35	32
Degraded and/or destroyed	69,400	89.8	53,500	69.3	86	78.6	66	61
Discharged to surface water and/or POTW	4,630	6	9,260	12	23	21.3	5	5
Adsorbed by sludge	-	-	480	0.6	-	-	2	2
Total amount of organic constituent initially released to WW (i.e., reported in raw WW)	77,300	100	77,300	100	109	100	108	100

Source: Reference 4.

Table 12-4

Estimates of Disposal Partitioning for Organic Constituents Released to Wastewater for Indirect Dischargers

Disposal Pathway of Organic Constituents Released to Wastewater (WW)	Subcategory A and C Indirect Dischargers				Subcategory B and D Indirect Dischargers			
	Detailed Questionnaire Response		WATER7 Results		Detailed Questionnaire Response		WATER7 Results	
	1,000 lbs / yr	% of Total Released	1,000 lbs / yr	% of Total Released	1,000 lbs / yr	% of Total Released	1,000 lbs / yr	% of Total Released
Emitted into air from WW	3,850	4.2	17,900	19.8	1,480	21	3,300	47
Degraded and/or destroyed	53,500	59.1	32,300	35.7	3,910	56	1,240	17.7
Discharged to surface water and/or POTW	33,200	36.6	39,300	43.4	1,590	23	2,380	34
Adsorbed by sludge	-	-	1,040	1.1	-	-	62	<1
Total amount of organic constituent initially released to WW (i.e., reported in raw WW)	90,500	100	90,500	100	6,980	100	6,980	100

Source: Reference 4.

Table 12-5

Increase in Criteria Pollutant Emissions from Steam Generation (tons/year)

Criteria Pollutant	Subcategory A and C Directs		Subcategory B and D Directs		Subcategory A and C Indirects		Subcategory B and D Indirects	
	BAT Opt. 2	BAT Opt. 3	BAT Opt. 2	BAT Opt. 3	PSES Opt. 1	PSES Opt. 2	PSES Opt. 1	PSES Opt. 2
CO	60	185	0	2	62	230	8	22
NO_x	450	1,390	1	12	468	1,730	56	167
VOC	12	39	0	0	13	48	1	5
SO_2	793	2,450	2	20	825	3,040	100	293
PM	77	238	0	2	80	295	9	28
Total	1,390	4,300	3	36	1,450	5,340	174	515

Source: Reference 5.

Table 12-6

Regulatory Impact on Solid Waste Generation

	Subcategory A and C Direct Dischargers	Subcategory B and D Direct Dischargers	Subcategory A and C Indirect Dischargers	Subcategory B and D Indirect Dischargers
Current dry sludge generated (tons/yr)	36,400	2,760	68,500	4,630
BAT/BPT/BCT Increase in dry sludge generation (tons/yr)	5,180	44	--	--
BAT/PSES Increase in waste solvent generation (tons/yr)	57,300	--	63,500	6,370
BAT/PSES Increase in waste HCl generation (tons/yr)	467	--	706	--

Table 12-7

Flow Sensitivity Analysis Results

Subcategory	Discharge Status	Percent of Process Wastewater Flow Requiring Treatment (a)	Electricity Use (1×10^6 kWh/yr)	Steam Use (1×10^6 kWh/yr)	Total Energy Use (1×10^6 kWh/yr)	Percentage of Industry Energy Purchase for 1990
A and C	Directs	100	13.6	2,220	2,240	24.9
		90	13.4	2,000	2,010	22.4
		80	13.1	1,780	1,790	19.9
		70	12.8	1,560	1,580	17.5
		60	12.8	1,340	1,350	15.1
		50	12.5	1,130	1,140	12.7
		40	12.3	905	917	10.2
		30	12.2	699	711	7.9
		20	12.0	472	484	5.4
		10	11.8	253	264	2.9
A and C	Indirects	100	5.26	2,750	2,760	30.8
		90	5.02	2,480	2,490	27.7
		80	4.81	2,210	2,220	24.7
		70	4.62	1,970	1,970	21.9
		60	4.45	1,690	1,690	18.8
		50	4.33	1,410	1,410	15.7
		40	4.29	1,150	1,160	12.9
		30	4.18	870	875	9.7
		20	4.10	588	592	6.6
		10	4.04	310	314	3.5
B and D	Indirects	100	1.50	266	268	3.0
		90	1.50	243	244	2.7
		80	1.48	216	217	2.4
		70	1.47	189	191	2.1
		60	1.45	163	164	1.8
		50	1.46	147	148	1.7
		40	1.45	118	119	1.3
		30	1.44	88.8	90.2	1.0
		20	1.45	60.5	62.0	0.7
		10	1.48	34.6	36.1	0.4

(a) Requiring treatment by in-plant steam stripping with distillation.

Table 12-8

Preliminary Impacts of Control Options for Subcategory A, B, C, and D Pharmaceutical Facilities Based on Process Area Streams

Control Option	VOHAP Conc. Cutoff(a) (ppmw)	Flow Cutoff (lpm)	Total Flow Controlled By Option (%)	HAP Emissions (mg/yr)	HAP Emission Reduction (%)	Total Annual Cost ($M/yr)	HAP Cost Effectiveness ($/mg HAP ER[b])
Baseline	-	-	-	12,500	-	-	-
1	1,000	10	46	1,650	87	19.0	1,750
2	800	5	47	1,640	87	19.8	1,830
3	500	1	72	1,520	88	26.1	2,380
4	200	1	75	1,510	88	27.6	2,520
5	100	1	80	1,500	88	29.5	2,680

(a) "VOHAP Conc. Cutoff" means the volatile organic HAP concentration determined by Method 305 in 40 CFR Part 63, Appendix A.
(b) "$/mg HAP ER" means the dollars per megagram of HAP emission reduction by the given control option, which is determined by dividing the annual cost of the option by the annual emission reduction.
All options include an action level of 10,000 ppmw volatile organic HAP concentration at any flow rate.
Total industry wastewater flow equals 75,300 liters per minute.

Table 12-9

Preliminary Impacts of Control Options for Subcategory A, B, C, and D Pharmaceutical Facilities Based on Disaggregated Streams

Control Option	VOHAP Conc. Cutoff(a) (ppmw)	Flow Cutoff (lpm)	Total Flow Controlled By Option (%)	HAP Emissions (mg/yr)	HAP Emission Reduction (%)	Total Annual Cost ($M/yr)	HAP Cost Effectiveness ($/mg HAP ER[b])
Baseline	-	-	-	12,500	-	-	-
1	1,000	10	7	2,790	78	6.6	680
2	800	5	10	2,440	80	8.0	800
3	500	1	16	2,120	83	10.6	1,020
4	200	1	25	1,680	87	13.7	1,270
5	100	1	29	1,630	87	15.9	1,460

(a) "VOHAP Conc. Cutoff" means the volatile organic HAP concentration determined by Method 305 in 40 CFR Part 63, Appendix A.
(b) "$/mg HAP ER" means the dollars per megagram of HAP emission reduction by the given control option, which is determined by dividing the annual cost of the option by the annual emission reduction.
All options include an action level of 10,000 ppmw volatile organic HAP concentration at any flow rate.
Total industry wastewater flow equals 75,300 liters per minute.

REFERENCES

1. U.S. Department of Commerce. 1990 Annual Survey of Manufacturers, Statistics for Industry Groups and Industries. M90(AS)-1, March 1992.

2. Test Methods for Evaluating Solid Waste, Physical/Chemical Methods, SW-846, 3rd Edition, May 1991.

3. U.S. EPA, Office of Air Quality Planning and Standards. Hazardous Waste Treatment, Storage, and Disposal Facilities (TSDF)--Air Emission Models. EPA-450/3-87-0, U.S. Environmental Protection Agency, Research Triangle Park, North Carolina, December 1987.

4. Memorandum: WATER7 Analysis of the Fate of Organic Pollutant Loads Through Pharmaceutical Facilities, from Radian Corporation to the Public Record, May 18, 1994.

5. Calculation of Air Emissions Related to Steam Generation. Prepared by R. Sieber, Radian Corporation. December 15, 1994.

6. U.S. EPA. Draft Hazardous Waste Minimization and Combustion Strategy. EPA Report No. 530-D-94-002, U.S. Environmental Protection Agency, Washington, D.C., May 1994.

7. U.S. EPA, Office of Solid Waste. Reengineering RCRA for Recycling. U.S. Environmental Protection Agency, Washington, D.C., April 22, 1994.

SECTION 13

BEST PRACTICABLE CONTROL TECHNOLOGY (BPT)

13.1 Introduction

Effluent limitations guidelines based on the best practicable control technology currently available establish quantitative limits on the direct discharge of pollutants from existing industrial point sources. BPT effluent limitations guidelines are based upon the average of the best existing performance, in terms of treated effluent discharged by facilities of various sizes, ages, and unit processes within a category or subcategory. BPT effluent limitations guidelines most commonly focus on the control of conventional and nonconventional pollutants, but can also control priority pollutants, such as cyanide.

BPT effluent limitations guidelines are based upon the performance of specific technologies, but do not require the use of any specific technology. BPT effluent limitations guidelines are applied to individual facilities through NPDES permits issued by EPA or authorized states under Section 402 of the CWA. The facility then chooses its own approach to comply with its permit limitations.

In developing BPT, the Agency considers the total cost of applying the technologies in relation to the effluent reduction benefits to be achieved from the technologies; the size and age of equipment and facilities; the processes used; the engineering aspects of applying various types of control techniques; process changes; and nonwater quality environmental impacts, including energy requirements.

The Agency proposes to establish BPT effluent limitations based on in-plant cyanide destruction and advanced biological treatment (BPT Option 2) for Subcategories A and C, and advanced biological treatment (BPT Option 2) for Subcategories B and D, as discussed in Section 11.

The following information is discussed in this section:

- Section 13.2 reviews the subcategories and the pollutants proposed to be regulated by BPT and presents the proposed BPT effluent limitations guidelines; and
- Section 13.3 discusses BPT effluent limitations guidelines implementation with regard to NPDES permits, point of application, and monitoring and compliance issues.

13.2 Summary of the Proposed BPT Effluent Limitations Guidelines

13.2.1 Regulated Subcategories

BPT effluent limitations guidelines, as discussed in Section 7.3, are proposed for Subcategories A, B, C, and D. As discussed in Section 4.3, Subcategories A, B, and C include wastewater discharges resulting from the manufacture of pharmaceuticals by fermentation, biological or natural extraction processes, and chemical synthesis processes, respectively. Subcategory D includes wastewater discharges resulting from mixing, compounding, and formulating of pharmaceutical products.

13.2.2 Regulated Pollutants

The proposed BPT effluent limitations guidelines establish BOD_5, COD, and TSS effluent limitations for Subcategories A, B, C, and D. In addition, cyanide is proposed to be regulated in Subcategory A and C wastewater discharges.

The pH effluent limit, established in the 1976 Final Rule (41 FR 50676) to be the range of 6.0 to 9.0 standard units for all subcategories, will not be amended. As discussed in Section 6.5, other conventional pollutants, such as fecal coliform and oil and grease, will not be regulated under BPT because they are not pollutants of concern for this industry.

13.2.3 The Proposed BPT Effluent Limitations Guidelines

The proposed BPT effluent limitations guidelines for each subcategory are based on a combination of long-term mean effluent concentrations and variability factors that account for day-to-day variation in measured treated effluent concentrations. Long-term means, discussed in Section 8, are target values that a facility's treatment system should achieve on a long- term, average basis. The variability factors, discussed in the Statistical Support Document (1), which is located in the Administrative Record for this rulemaking, represent the ratio of an elevated value that would be expected to occur only rarely to the long-term mean. The variability factors are provided in Appendix C of the Technical Development Document for ease of reference. The purpose of the variability factor is to allow for variations in effluent concentrations that comprise the long-term mean. A facility that designs and operates its treatment system to achieve a long-term mean on a consistent basis should be able to comply with the daily and monthly limitations in the course of normal operations.

Table 13-1 presents the proposed maximum daily and monthly average BPT effluent limitations guidelines for end-of-pipe monitoring points for Subcategories A, B, C, and D based on long-term mean treatment performance concentrations and associated variability factors.

The limitations for each pollutant were calculated in the following manner. For each available data set from best-performing advanced biological treatment systems, the long-term mean concentration was multiplied by the 1-day and 30-day variability factors for the data set. This resulted in dataset specific limitations. The mean value of the dataset specific limitations, calculated from all available datasets, was established. The mean value based on the 1-day variability factor is the BPT maximum limitation for any one day, the mean value based on the 30-day variability factor is the BPT monthly average limitation.

13.3 Implementation of the BPT Effluent Limitations Guidelines

13.3.1 NPDES Permit

BPT effluent limitations guidelines are applied to individual facilities through NPDES permits issued by EPA or authorized states under Section 402 of the CWA.

The proposed effluent limitations guidelines are concentration-based and, as such, do not regulate wastewater flow. For in-plant effluent limitations, the concentration-based limitations will apply directly to applicable in-plant streams. For end-of-pipe effluent limitations, permit writers will use a reasonable estimate of process wastewater discharge flow and the concentration-based limitations to develop mass-based limitations for the NPDES permit.

"Process wastewater discharge" is defined by 40 CFR 122.2 to include wastewaters resulting from manufacture of pharmaceutical products that come in direct contact with raw materials, intermediate products, and final products, and surface runoff from the immediate process area that has the potential to become contaminated. Noncontact cooling waters, utility wastewaters, general site surface runoff, groundwater, and other nonprocess water generated on site are specifically excluded from this definition. The appropriate process wastewater discharge flow to be used when developing mass-based limitations must be determined by the permitting or control authority on a case-by-case basis using current information provided by the applicant. In cases where the permit writer deems the process wastewater discharge flow claimed by industry to be excessive, he/she may develop a more appropriate process wastewater discharge flow for use in computing the mass effluent limitations. The permit writer should review the following items to evaluate whether process wastewater discharge flow is excessive.

- Component flows, to ensure that the claimed flows are, in fact, process wastewater discharge flows as defined by 40 CFR 122.2.

- Plant operations, to ensure that sound water conservation practices are being followed. Examples include minimization of process water uses and reuse or recycle of intermediate process waters or treated wastewaters at the process area and in wastewater treatment operations (pump seals, equipment and area washdowns, etc.).

- The barometric condenser use at the process level. Often, barometric condensers will generate relatively large volumes of slightly contaminated water. Replacing barometric condensers with surface condensers can reduce wastewater volumes significantly and result in collection of condensates that may be returned to the process.

To establish an NPDES permit for a direct discharger, the permit writer should determine the facility's subcategorization and use the corresponding concentration-based effluent limitations as a basis for developing the mass-based limitations. The permit writer should then use best professional judgment to determine the facility's annual average process wastewater discharge flow (i.e., the permit writer should consider only the sources of "process wastewater discharge," as defined previously, when determining the annual average process wastewater discharge flow; nonprocess wastewater discharges should not be included). The annual average flow is defined as the average of daily flow measurements calculated over at least a year; however, if available, three to five years of data are preferable to obtain a representation of average daily flow. (2)

If no historical or actual process wastewater flow data exist, the permitting authority is advised to establish a reasonable estimate of the facility's projected flow that would be representative during the entire term of the permit. This may include a request for the facility to measure process wastewater flows for a representative period of time to establish a flow basis. If a plant is planning significant changes in production during the effective period of the permit, the permitting authority may consider establishing multiple tiers of limitations as a function of these production changes. Alternatively, a permit may be modified during its term, either at the request of the permittee or another interested party, or on EPA's initiative, to increase or decrease the flow basis in response

to a significant change in production (40 CFR 124.5, 122.62). A change in production may be an "alteration" of the permitted activity or "new information" that could provide the basis for a permit modification (40 CFR 122.62(a)).

After determining the facility's annual average process wastewater flow, the permit writer should use the annual average process wastewater discharge flow to convert the end-of-pipe concentration-based limitations into mass-based limitations. Below is an example of how to convert a concentration-based limitation into a mass-based limitation: the conversion of the maximum monthly average discharge of TSS for a hypothetical facility with Subcategory A and B operations. The facility's average daily wastewater (WW) generation in gallons per day is as follows:

- 1,000,000 gal/day of Subcategory A pharmaceutical process WW;
- 339,000 gal/day of Subcategory B pharmaceutical process WW;
- 2,718,000 gal/day of noncontact cooling WW; and
- 11,000 gal/day of sanitary WW.

Totalling the amounts listed above, the facility generates approximately 4,068,000 gal/day of wastewater. To estimate the process wastewater discharge, the permit writer should review the component flows listed above and determine which wastewater flows can be deemed process wastewater discharge. In this case, only Subcategory A and B pharmaceutical process wastewater constitute process wastewater discharge. Allowance would not be given for noncontact cooling wastewater or sanitary wastewater. Thus, a reasonable estimate of the process wastewater discharge for this hypothetical facility is calculated as follows:

Process WW discharge = Subcategory A pharmaceutical process WW + Subcategory B pharmaceutical process WW

= 1,000,000 GPD + 339,000 gal/day

= 1,339,000 gal/day

For Subcategory A wastewater discharges, the concentration-based effluent limitation for the maximum daily discharge of TSS, as presented in Table 13-1, is 318 mg/L. For Subcategory B wastewater discharges the concentration-based effluent limitation for the maximum daily discharge of TSS is 80 mg/L. The permit writer would convert these concentration-based limitations into a mass-based limitation by using the following equation:

$$L_M = L_C \times F \times k \qquad (13\text{-}1)$$

where:
- L_M = mass-based effluent limitation, lbs/day
- L_C = concentration-based effluent limitation, mg/L
- F = average subcategory process wastewater discharge, gal/day
- k = unit conversion factor.

For this example, the unit conversion factor, k, is used to convert from [(mg/L) × (gal/day)] to (lbs/day) as follows:

$$k = (mg/L) \times (1\,L/0.264179\,gal) \times (1\,g/1000\,mg) \times (1\,lb/453.592\,g) \times (gal/day) = 8.345 \times 10^{-6}$$

For the example, the mass-based maximum daily TSS limitation would be calculated using equation (13-1) as follows:

For Subcategory A process wastewaters:

$$L_M = (318\,mg/L\,TSS) \times (1{,}000{,}000\,gal/day) \times 8.345 \times 10^{-6}$$
$$L_M = 2{,}654\,lbs/day\,TSS$$

For Subcategory B process wastewaters:

$$L_M = (80\ mg/L\ TSS) \times (339{,}000\ gal/day) \times 8.345 \times 10^{-6}$$
$$L_M = 226\ lbs/day\ TSS$$

Thus, the mass-based maximum daily TSS limitation would be the sum of 2,654 lbs/day TSS and 226 lbs/day TSS which is 2,880 lbs/day TSS.

Limits for other end-of-pipe parameters would be calculated in a similar manner.

Additional detailed guidance on the establishment of permit limitations is available in the Guidance for Implementing the Pharmaceutical Manufacturing Industry Regulations, included as Appendix A.

13.3.2 Point of Application

The proposed BPT effluent limitations guidelines for cyanide in wastewater for Subcategory A and C operations are applicable to the in-plant cyanide-bearing wastewater streams. The proposed BPT effluent limitations guidelines for BOD_5, COD, and TSS for Subcategory A, B, C, and/or D direct dischargers would be applicable to the final effluent at the point of discharge to waters of the United States (i.e., end-of-pipe).

13.3.3 Monitoring and Compliance

The proposed BPT effluent limitations guidelines for Subcategory A, B, C, and/or D direct dischargers require daily monitoring for BOD_5, COD, and TSS. For facilities with Subcategory A and/or C operations, cyanide-bearing wastestreams would require monitoring on each cyanide destruction treatment batch.

Compliance with the proposed end-of-pipe effluent limitations guidelines should be determined by multiplying the measured concentration of a regulated pollutant in the effluent sample by a conversion factor and the total applicable process wastewater flow discharged during the effluent sampling period, which is typically 24 hours. Thus, the mass compliance value should be based on the applicable flow discharged on the day of sampling, not on the long-term average flow rate that provided the basis for establishing the permit limitations and standards. The mass compliance value can be determined using the following equation:

$$CV_M = P_C \times F \times k \qquad (13\text{-}2)$$

where:

CV_M	=	mass compliance value, lbs/day
P_C	=	pollutant concentration, mg/L
F	=	average applicable process wastewater discharge flow over 24-hour sampling period, gal/day
k	=	unit conversion factor, 8.345×10^{-6}.

For example, if analytical data from a 24-hour sampling period for the facility in the above example demonstrates a TSS concentration of 70 mg/L, and the measured applicable process wastewater flow discharged for the same 24-hour period is 4.1 million gallons, then the plant's reported daily mass compliance value of the pollutant, using Equation 13-2, is 2,395 lbs/day. Similarly, the monthly average compliance value would be calculated by averaging the available daily mass compliance values in each calendar month.

Table 13-1

Proposed BPT Effluent Limitations Guidelines for Direct Dischargers

Subcategory	Pollutant or Pollutant Property	Proposed BPT Effluent Limitation for End-of-Pipe Monitoring Points (a)	
		Maximum for any one day (mg/L)	Monthly Average (mg/L)
A - Fermentation Operations	BOD_5	137	58
	COD	1,100	628
	TSS	318	110
	Cyanide	0.766	0.406
B - Biological and Natural Extraction Operations	BOD_5	37	11
	COD	145	60
	TSS	80	27
C - Chemical Synthesis Operations	BOD_5	137	58
	COD	1,100	628
	TSS	318	110
	Cyanide	0.766	0.406
D - Mixing, Compounding, or Formulating Operations	BOD_5	37	11
	COD	145	60
	TSS	80	27

(a)The proposed BPT limitations for cyanide apply at an in-plant location (i.e., prior to dilution with non-cyanide-bearing wastestreams).

REFERENCES

1. U.S. EPA, Office of Water. Statistical Support Document for the Proposed Effluent Limitations Guidelines for the Pharmaceutical Manufacturing Industry. U.S. Environmental Protection Agency, Washington, D.C., February 10, 1995.

2. U.S. EPA, Office of Water. Training Manual for NPDES Permit Writers. EPA 833-B-93-003, U.S. Environmental Protection Agency, Washington, D.C., 1993.

SECTION 14

BEST CONVENTIONAL TECHNOLOGY

14.1 Introduction

Effluent limitations guidelines based on best conventional technology establish quantitative limits on the direct discharge of conventional pollutants from existing industrial point sources. In contrast to BPT guidelines, which are based on the average of the best existing performance by a group of facilities, BCT guidelines are developed by identifying candidate technologies and evaluating their cost-reasonableness. Effluent limitations guidelines based upon BCT may not be less stringent than BPT effluent limitations guidelines. As such, BPT effluent limitations are a "floor" below which BCT efficient limitations guidelines cannot be established. As discussed below, EPA has developed a BCT cost test methodology to assist the Agency in determining whether it is "cost-reasonable" for industry to control conventional pollutants at a level more stringent than would be required by BPT effluent limitations.

The following information is presented in this section:

- Section 14.2 discusses the Agency's general methodology for determining BCT effluent limitations for industry;
- Section 14.3 reviews the subcategories and pollutants proposed to be regulated by BCT, describes the application of the general BCT methodology to the pharmaceutical manufacturing industry, and presents the proposed BCT effluent limitation guidelines; and
- Section 14.4 discusses BCT effluent limitations guideline implementation.

14.2 General Methodology for BCT Effluent Limitations Development

The July 9, 1986 Federal Register (51 FR 24974) presents the Agency's general methodology for developing BCT effluent limitations guidelines. BCT effluent limitations guidelines are based on the performance of the pollution control technology selected as BCT. As noted in 51 FR 24974, the first step in determining BCT is to establish that a BCT option is technologically feasible (defined as providing conventional pollutant control beyond the level of control provided by application of BPT). If a BCT option is found to be technologically feasible, the Agency applies a two-part BCT cost test to evaluate the "cost-reasonableness" of the BCT option. The BCT cost test consists of a POTW test and an industry cost-effectiveness test that the BCT option must pass to be considered as a basis for BCT effluent limitations guidelines. The results of these tests along with other industry-specific factors are evaluated to determine BCT. The POTW cost test, the industry cost-effectiveness test, and the process of BCT determination are discussed below.

14.2.1 POTW Cost Test

The POTW cost test compares the cost-effectiveness of an industrial treatment system upgrade to meet the BCT requirements to the benchmark cost-effectiveness of a POTW upgrade. For a BCT option to pass the POTW cost test, the cost per pound of conventional pollutant removed by upgrading from BPT to the BCT option at industrial direct dischargers must be less than the cost per pound of conventional pollutant removed by upgrading POTWs from secondary treatment to advanced secondary treatment. Specifically, the upgrade cost to industry must be less than the POTW benchmark of $0.25 per pound (in 1976 dollars) for industries whose cost per pound is based on long-term performance data (Tier I POTW benchmark), or must be less than $0.14 (in 1976 dollars) per pound for industries whose cost per pound is not based on long-term performance data (Tier II POTW benchmark).

As noted in 51 FR 24974, the conventional pollutants measured for removal during the two-part BCT cost test are BOD_5 and TSS. Oil and grease may be used along with BOD_5 and TSS to calculate pollutant removal for BCT options when deemed appropriate for the industry and technology being evaluated. Fecal coliform and pH are not included in the calculations because control of these pollutants is not measurable as "pounds removed". An acceptable interval for controlling pH is evaluated with respect to the particular processes of a BCT option. Generally, the acceptable pH interval for BCT will be the same as that for BPT. Maintaining the acceptable interval is an inherent cost of the BCT option and must be economically achievable and cost-reasonable (51 FR 24974).

14.2.2 Industry Cost-Effectiveness Test

To remain a viable option, a BCT option must also pass an industry cost-effectiveness test which consists of computing a ratio of two incremental costs. The first increment is the cost per pound of pollutant load removed by the BCT option relative to BPT; the second increment is the cost per pound of pollutant load removed by BPT relative to no treatment (i.e., raw wastewater). The ratio of the two incremental costs (first cost divided by the second cost) is compared to an industry benchmark. The industry benchmark is a ratio of two POTW incremental costs: (1) the cost per pound of pollutant removed for a POTW to upgrade from secondary treatment to advanced secondary treatment, and (2) the cost per pound of pollutant removed for a POTW to upgrade from no treatment to secondary treatment. If the first ratio (BCT option to BPT) is lower than the industry benchmark, the BCT option passes the industry cost-effectiveness test. The Tier I industry benchmark, for industries whose ratio is based on long-term performance data, is 1.29. The Tier II industry benchmark, for industries whose ratio is not based on long-term performance data, is 0.68.

In calculating the ratio of a BCT option to BPT, the Agency will consider any BCT option cost per pound less than $0.01 to be equivalent to zero costs. The Agency

believes that a BCT option with zero cost per pound of pollutant removed satisfies the Congressional intent for cost-reasonableness.

14.2.3 BCT Determination

BCT is determined by evaluating results of both the POTW test and the industry cost-effectiveness test as measures of cost-reasonableness. In addition, Section 304 (b)(4)(B) of the CWA instructs the Agency to consider "other factors deemed appropriate" when making BCT determinations; other factors are considered on an industry-specific basis. Generally, BCT is the most stringent technology option (i.e., the technology option that achieves the greatest pollutant reduction) to pass both parts of the cost test. If all BCT options for an industry category or subcategory fail either or both of the tests, or if no BCT option more stringent than BPT is identified, then BCT is set equal to BPT.

The owners or operators of facilities subject to BCT are not required to use the specific technologies selected by EPA to establish BCT, but may choose to use any combination of process technologies and wastewater treatment to comply with NPDES permit limitations derived from BCT effluent limitations guidelines.

14.3 BCT Effluent Limitations Guidelines Development for the Pharmaceutical Manufacturing Industry

14.3.1 Regulated Subcategories

BCT effluent limitations guidelines, as discussed in Section 7.3, are being proposed for Subcategories A, B, C, and D.

14.3.2 Regulated Pollutants

The proposed BCT effluent limitations guidelines establish BOD_5 and TSS effluent limitations. The pH effluent limitation under BCT will be the equivalent of the pH limitation established by BPT. An effluent limitations guideline for oil and grease will not be proposed since oil and grease is not normally found in pharmaceutical manufacturing waste streams.

14.3.3 Application of General BCT Methodology to the Pharmaceutical Manufacturing Industry

The Agency applied the general methodology for BCT effluent limitations guidelines development to the pharmaceutical manufacturing industry subcategories. First, technologically feasible BCT options that provide a greater degree of conventional pollutant control than BPT were identified. Section 7.3.2 describes the BCT options evaluated by the BCT determination process. After determining that the BCT options were technologically feasible, the Agency applied the two-part BCT cost test. The results of the BCT cost test were used to establish the technology basis for the proposed BCT effluent limitations guidelines.

The following subsections discuss the BPT baseline established for the two-part BCT cost test, the BCT options evaluated, the use of the pharmaceutical cost model to generate costs for this analysis, the two-part BCT cost test results, and the proposed BCT effluent limitations guidelines for the pharmaceutical manufacturing industry subcategories.

14.3.3.1 BCT Cost Test Baseline

To apply the two-part BCT cost test to the pharmaceutical manufacturing industry, a baseline technology representing BPT was defined to serve as the comparison point for the more stringent BCT options. The methodology for BCT determination (as

documented in 51 FR 24974) requires that this point of comparison is BPT. As discussed in Section 13, BPT Option 2, advanced biological treatment, is the proposed BPT Option for Subcategories A and C and Subcategories B and D. Thus, the baseline technology used in the two-part BCT cost test is advanced biological treatment.

14.3.3.2 BCT Options

Subcategories A and C

As described in Section 7.3.2, there are five BCT options for Subcategories A and C:

- Option 1 = Existing Biological Treatment;
- Option 2 = Advanced Biological Treatment;
- Option 3 = Option 2 + Effluent Filtration;
- Option 4 = Option 2 + Polishing Pond; and
- Option 5 = Option 2 + Polishing Pond + Effluent Filtration.

These five BCT options are equivalent to the five BPT options for Subcategories A and C, except for cyanide treatment, which is not included under BCT because cyanide is not a conventional pollutant. BCT Option 1 is equivalent to BPT Option 1 and represents a no cost, no load removal option. BCT Option 2 is equivalent to the baseline BPT technology proposed (BPT Option 2) and BCT Option 2 forms the comparison point for the BCT cost test.

Subcategories B and D

As described in Section 7.3.2, there are three BCT options for Subcategories B and D:

- Option 1 = Existing Biological Treatment;
- Option 2 = Advanced Biological Treatment; and
- Option 3 = Option 2 + Effluent Filtration.

These three BCT options are equivalent to the three BPT options for Subcategories B and D. BCT Option 1 is equivalent to BPT Option 1 and represents a no cost, no load removal option. BCT Option 2 is equivalent to the baseline BPT technology proposed (BPT Option 2) and Option 2 thus forms the comparison point for the BCT cost test.

14.3.3.3 Pharmaceutical Manufacturing Cost Model

The Agency used the pharmaceutical manufacturing cost model (described in Section 10) to calculate baseline (BPT Option 2) conventional pollutant control costs and corresponding costs for the BCT options. Since BCT options primarily target BOD_5 and TSS reductions, only BOD_5 and TSS pollutant control costs were calculated by the cost model. Annualized conventional pollutant control costs for the baseline and BCT options were calculated in 1990 dollars using a 11.4% interest rate and a 20-year equipment lifetime for pollution control equipment.

14.3.3.4 BCT Cost Test Results

Table 14-1 summarizes the results of the two-part BCT cost test. All results are based on the use of long-term performance (i.e., Tier I) data. Results of the POTW cost test and the industry cost-effectiveness test are discussed below.

POTW Cost Test Results

Results of the POTW cost test are summarized in the upper portion of Table 14-1. For Subcategory A and C direct dischargers, BCT Options 3, 4, and 5 failed the POTW cost test. For Subcategory B and D direct dischargers, BCT Option 3 failed the POTW cost test.

As an example of POTW test application, consider BCT Option 3 for Subcategory A and C direct dischargers. The cost of upgrading from the BPT baseline (advanced

biological treatment) to BCT Option 3 (advanced biological treatment followed by effluent filtration) is $1,870,000 per year (in 1990 dollars). The load reduction of BOD_5 and TSS achieved by upgrading to BCT Option 3 is 925,000 lbs/yr. Thus, upgrading from the BPT baseline to BCT Option 3 results in a ratio of 2.02 $/lb (dollars expended to pounds of BOD_5 and TSS removed). This ratio is greater than the Tier I POTW benchmark (in 1990 dollars) of 0.56 $/lb. (The POTW benchmark of 0.56 $/lb, expressed in 1990 dollars, was calculated using the May 1986 promulgated methodology entitled BCT Benchmarks: Methodology, Analysis and Results for Calculating and Indexing BCT POTW Benchmarks to Various Years' Dollars [1].) Since the cost per pound of pollutant removed is greater than the POTW benchmark, BCT Option 3 for Subcategory A and C direct dischargers failed the POTW cost test.

Industry Cost-Effectiveness Test Results

Results of the industry cost-effectiveness test are presented in the lower portion of Table 14-1. For Subcategory A and C direct dischargers, BCT Options 3, 4, and 5 failed the industry cost-effectiveness test. For Subcategory B and D direct dischargers, BCT Option 3 failed the industry cost-effectiveness test.

As an example of industry cost-effectiveness test application, consider BCT Option 3 for Subcategory A and C direct dischargers. From the POTW test, the incremental cost per pound of pollutant removed associated with upgrading from the BPT baseline to BCT Option 3 was 2.02 $/lb. The cost of upgrading from no treatment (i.e., raw wastewater) to the BPT baseline is $29,100,000 per year (in 1990 dollars). The load reduction of BOD_5 and TSS achieved by upgrading from no treatment to the BPT baseline is 101,000,000 lbs/yr. Thus, the incremental cost per pound of pollutant load removed for Subcategory A and C direct dischargers upgrading from no treatment to the BPT baseline is 0.29 $/lb. The ratio of these two incremental costs is 6.97 (i.e., 2.02 divided by 0.29). Since this ratio (6.97) is greater than the industry benchmark of 1.29, BCT Option 3 failed the industry cost-effectiveness test.

14.3.3.5 Conclusions

Based on the results of the two-part BCT cost test and the criteria discussed in Section 14.1.3 for BCT determination, the proposed BCT effluent limitations guidelines for Subcategory A and C and Subcategory B and D direct dischargers are presented below.

BCT Determination for Subcategories A and C

For Subcategory A and C direct dischargers, BCT Options 3, 4, and 5 failed the two-part BCT cost test. Therefore, the proposed BCT is established as BCT Option 2, the equivalent of proposed BPT. As such, the proposed BCT for Subcategories A and C consists of advanced biological treatment. Table 14-2 presents the proposed BCT effluent limitations guidelines for Subcategories A and C.

BCT Determination for Subcategory B and D

For Subcategory B and D direct dischargers, BCT Option 3 failed the two-part BCT cost test. Therefore, the proposed BCT is established as BCT Option 2, the equivalent of proposed BPT. As such, the proposed BCT for Subcategories B and D consists of advanced biological treatment. Table 14-3 presents the proposed BCT effluent limitations guidelines for Subcategory B and D direct dischargers.

14.4 Implementation of the BCT Effluent Limitation Guidelines

The proposed BCT limitations for BOD_5 and TSS are equivalent to the proposed BPT limitations, and would be implemented in a manner similar to that described in Section 13.3.

Table 14-1

Summary Results of BCT Cost Test
(Monetary Values are 1990 $)

	POTW Cost Test			
	BPT Baseline to BCT Option 3		BPT Baseline to BCT Option 4	BBPT Baseline to BCT Option 5
	Subcategory A and C	Subcategory B and D	Subcategory A and C	Subcategory A and C
Annualized Cost for BOD & TSS Reduction ($/yr.)	1,870,000	541,000	17,500,000	20,800,000
BOD & TSS Load Red. (lbs./yr.)	925,000	31,000	1,460,000	3,120,000
($/lb.)	2.02	17.4	12.0	6.69
POTW Benchmark ($/lb.) 1990 $	0.56	0.56	0.56	0.56
Pass/Fail	Fail	Fail	Fail	Fail

	Industry Cost - Effectiveness Test			
	Raw WW to BPT Baseline = BPT Option 2		Raw WW to BPT Baseline = BPT Option 2	Raw WW to BPT Baseline = BPT Option 2
	Subcategory A and C	Subcategory B and D	Subcategory A and C	Subcategory A and C
Annualized Cost for BOD & TSS Reduction ($/yr.)	29,100,000	2,630,000	29,100,000	29,100,000
BOD & TSS Load Red. (lbs./yr.)	101,000,000	1,310,000	101,000,000	101,000,000
($/lb.)	0.29	2.00	0.29	0.29
Ratio	6.97	8.72	41.3	23.1
Ratio Benchmark	1.29	1.29	1.29	1.29
Pass/Fail	Fail	Fail	Fail	Fail

Notes:

Baseline is set equivalent to proposed BPT Option 2. The raw to baseline and baseline to BCT option costs and load reductions were developed using the pharmaceutical manufacturing cost model. These costs do not include costs for COD removal.

To adjust the POTW benchmark to 1990 dollars, the Agency used the promulgated methodology, BCT Benchmarks: Methodology, Analysis and Results, May 1986, for calculating and indexing BCT POTW benchmarks to various years' dollars (1).

Table 14-2

Proposed BCT Effluent Limitations Guidelines for Subcategory A and C Discharges

Pollutant	Proposed BCT Effluent Limitations	
	Maximum for Any One Day (mg/L)	Maximum for Monthly Average (mg/L)
BOD_5	137	58
TSS	318	110

Table 14-3

Proposed BCT Effluent Limitations Guidelines for Subcategory B and D Discharges

Pollutant	Proposed BCT Effluent Limitations	
	Maximum for Any One Day (mg/L)	Maximum for Monthly Average (mg/L)
BOD_5	37	11
TSS	80	27

REFERENCES

1. U.S. EPA. BCT Benchmarks: Methodology, Analysis, and Results for Calculating and Indexing BCT POTW Benchmarks to Various Year's Dollars. U.S. Environmental Protection Agency, Washington, D.C., May 1986.

SECTION 15

BEST AVAILABLE TECHNOLOGY ECONOMICALLY ACHIEVABLE (BAT)

15.1 Introduction

Effluent limitations guidelines based on the best available technology economically achievable establish quantitative limits on the direct discharge of priority and nonconventional pollutants to waters of the United States. These limits are based upon the performance of specific technologies, but do not specify which technologies must be used to achieve compliance. BAT effluent limitations guidelines are applied to individual facilities through NPDES permits issued by EPA or authorized states under Section 402 of the CWA. Each facility then chooses its own approach to comply with its permit limitations.

The technology selected by the Agency to define the BAT performance may include end-of-pipe treatment, process changes, and internal controls, even when these technologies are not common industry practice. BAT performance is established for groups of facilities with shared characteristics. Where a group of facilities demonstrates uniformly inadequate performance in controlling pollutants of concern, BAT may be transferred from a different subcategory or industrial category. Section 7 provides an overview of the technologies assessed by the Agency.

The Agency has selected in-plant steam stripping and cyanide destruction followed by end-of-pipe advanced biological treatment (BAT Option 2) as the technology basis for the proposed BAT effluent limitations guidelines for Subcategory A and/or Subcategory C direct dischargers. The Agency has selected end-of-pipe advanced biological treatment (BAT Option 1) as the technology basis for the proposed BAT effluent limitations guidelines for Subcategory B and/or Subcategory D direct dischargers. The rationale behind these selections is discussed in Section 11.

The following information is presented in this section:

- Section 15.2 reviews the subcategories and the pollutants proposed to be regulated by BAT and presents the proposed BAT effluent limitations guidelines; and
- Section 15.3 discusses BAT effluent limitations guidelines implementation with regard to point of application, NPDES permits, and monitoring and compliance issues.

15.2 Summary of the Proposed BAT Effluent Limitations Guidelines

15.2.1 Regulated Subcategories

Revised BAT effluent limitations guidelines are proposed for Subcategories A, B, C, and D. As discussed in Section 4.3, Subcategories A, B, and C include wastewater discharges resulting from the manufacture of pharmaceuticals by fermentation, biological or natural extraction processes, and chemical synthesis processes, respectively. Subcategory D includes wastewater discharges resulting from mixing, compounding, and formulating of pharmaceutical products.

15.2.2 Regulated Pollutants

The proposed BAT guidelines establish effluent limitations for the priority and nonconventional pollutants listed in Table 15-1 for direct dischargers in Subcategories A, B, C, and D. In addition, the proposed BAT guidelines establish effluent limitations for ammonia and cyanide for direct dischargers in Subcategories A and C. Conventional pollutants are regulated under BPT and BCT and not discussed here.

15.2.3 The Proposed BAT Effluent Limitations Guidelines

The proposed BAT effluent limitations guidelines for each subcategory are based on a combination of long-term mean treatment performance concentrations and variability factors that account for day-to-day variation in measured treated effluent concentrations. Long-term mean treatment performance concentrations, discussed in Section 8, are target values that a facility's treatment system should achieve on a long-term, average basis. The variability factors, discussed in the Statistical Support Document [1], which is located in the Record for this rulemaking, represent the ratio of an elevated value that would be expected to occur only rarely to the long-term mean. The purpose of the variability factor is to allow for variations in effluent concentrations that comprise the long-term mean. A facility that designs and operates its treatment system to achieve a long-term mean on a consistent basis should be able to comply with the daily and monthly limitations in the course of normal operations.

Tables 15-2 and 15-3 present the proposed maximum daily and monthly average BAT effluent limitations guidelines for Subcategory A and C operations, and Subcategory B and D operations, respectively. These proposed limitations were determined by multiplying the long-term means (LTMs) for each subcategory by the respective pollutant's 1-day and 4-day variability factors (VFs). Note that a 4-day variability factor is used for the proposed BAT limitations while a 30-day variability factor is used for the proposed BPT limitations. This results from the recommended daily monitoring frequency to show compliance with the proposed BPT BOD_5, COD, and TSS limitations and the weekly monitoring frequency to show compliance with the proposed BAT limitations.

The proposed regulation for the pharmaceutical manufacturing industry presents analytical method minimum levels in Section 439.1 (g). These values apply to those limitations and standards set at ND. For ease of use, the tables presented in this section

present the analytical method minimum level in parentheses for those limitations and standards set at ND.

15.3 Implementation of the BAT Effluent Limitations Guidelines

The proposed BAT effluent limitations are dependent on the type of manufacturing operations at each pharmaceutical manufacturing facility. The proposed effluent limitations for wastewater from Subcategory A and C operations are numerically different than the proposed effluent limitations for wastewater from Subcategory B and D operations. The proposed BAT Effluent Limitations Guidelines for Subcategory A and C operations are presented in Table 15-2. The proposed BAT Effluent Limitations Guidelines for Subcategory B and D operations are presented in Table 15-3.

As noted in Section 7, EPA is not proposing but is considering use of Best Management Practices (BMPs) to reduce discharges from leaks and spills of process chemicals and materials. These materials include organic solvents (some of which are ignitable) that contribute to air emissions and to effluent discharges and off-specification products which may upset biological treatment systems. BMPs may offer the opportunity to reduce these discharges and air emissions while concurrently increasing utilization of consumable materials. Suggested details on BMPs being considered for the pharmaceutical manufacturing industry are presented in Appendix B.

15.3.1 Establishing List of Pollutants for Compliance Monitoring

If final effluent limitations are promulgated as proposed, permit limitations would be established and compliance monitoring required for each regulated pollutant listed on Table 15-1 generated or used at a pharmaceutical manufacturing facility. Limitations and routine compliance monitoring would not be required for regulated pollutants not generated or used at a facility. A determination that regulated pollutants are not generated or used would be based on a review of all raw materials used and an

assessment of all chemical processes used, considering resulting products and by-products. The determination that a regulated pollutant is not generated or used would need to be confirmed by annual chemical analyses of wastewater from each monitoring location. Such confirmation would be provided by an analytical measurement of a non-detect value.

15.3.2 Point of Application

The proposed BAT limitations for cyanide presented in Table 15-2 are applicable to those wastewaters from Subcategory A and C operations known or believed to contain cyanide. Compliance monitoring for cyanide would occur in plant, prior to dilution or mixing with any non-cyanide-bearing wastewater. In-plant monitoring would be required to prevent compliance through dilution with non-cyanide-bearing wastewater.

The proposed BAT effluent limitations for ammonia (applicable to Subcategories A and C), and the organic pollutants listed in Tables 15-2 and Table 15-3 are end-of-pipe limitations and would be applicable to the final effluent at the point of discharge to waters of the United States. This compliance point is identical to the point used to demonstrate compliance with the proposed BPT effluent limitations guidelines.

EPA also is soliciting comments and data on whether limits for the 12 most strippable priority and nonconventional organic pollutants should be applied at an in-plant monitoring point (e.g., following steam stripping and prior to dilution with other process and non-process wastewaters not containing these pollutants in treatable quantities and prior to end-of-pipe biological treatment systems). The limits EPA would propose for this in-plant monitoring point are found in Table 2-8.

15.3.3 Permit Limitations

EPA expects that permit limitations for cyanide at in-plant locations based on the proposed BAT limitations would be concentration-based, and would not be converted to a mass basis. Table 15-2 lists these proposed concentration-based limitations, which apply only to Subcategories A and C. A concentration basis should be used because it offers a direct benchmark to assess whether the in-plant control technology is achieving the intended BAT level. In-plant wastestreams that require control may be generated or treated on a variable, batch basis. In such a setting, mass-based permit limitations are difficult to establish accurately, and compliance is hindered because the permitted facility cannot make a direct measurement to determine if its control technology is performing at the required level. Concentration-based permit limitations eliminate these problems and offer a direct measure to both the permitting authority and the permitted facility that BAT performance levels are being achieved.

End-of-pipe permit limitations based on the proposed BAT limitations for ammonia (for Subcategories A and C) and organic constituents would be mass-based unless the maximum for any one day limitation is non-detect (ND). In such a case, the permit would specify that all measured values should be non-detect values. Non-detect values are concentration-based measurements reported below the minimum level that can be reliably measured by the analytical method for the pollutant. The minimum level is the level at which an analytical system gives recognizable signals and an acceptable calibration point. Minimum levels for all regulated pollutants are specified in Table 18-7.

If final effluent limitations are promulgated as proposed, permit writers would use a reasonable estimate of process wastewater discharge flow and the concentration-based limitations listed in Table 15-2 to develop mass-based limitations for the NPDES permit. "Process wastewater discharge" is defined by 40 CFR 122.2 to include wastewaters resulting from pharmaceutical products manufacturing that come in direct contact with

raw materials, intermediate products, and final products, and surface runoff from the immediate process area that has the potential to become contaminated. Noncontact cooling waters, utility wastewaters, general site surface runoff, groundwater, and other nonprocess water generated on site are specifically excluded from this definition. The appropriate process wastewater discharge flow to be used when developing mass-based limitations must be determined by the permitting or control authority on a case-by-case basis using current information provided by the applicant. In cases where the permit writer deems the process wastewater discharge flow claimed by industry to be excessive, he/she may develop a more appropriate process wastewater discharge flow for use in computing the mass-based limitations. The permit writer should review the following items to evaluate whether process wastewater discharge flow is excessive:

- Component flows, to ensure that the claimed flows are, in fact, process wastewater discharge flows as defined by 40 CFR 122.2.
- Plant operations, to ensure that sound water conservation practices are being followed. Examples include minimizing process water uses and reusing or recycling intermediate process waters or treated wastewaters at the process area and in wastewater treatment operations (pump seals, equipment and area washdowns, etc.).
- The barometric condenser use at the process level. Often, barometric condensers will generate relatively large volumes of slightly contaminated water. Replacing barometric condensers with surface condensers can reduce wastewater volumes significantly and result in collection of condensates that may be returned to the process.

Once the permit writer has reviewed the permit application, best professional judgment should be used to determine the facility's annual average process wastewater discharge flow (i.e., the permit writer should consider only the sources of "process wastewater discharge," as defined previously, when determining the annual average process wastewater discharge flow; nonprocess wastewater discharges should not be included). The annual average flow is defined as the average of daily flow measurements calculated

over at least a year; however, if available, three to five years of data are preferable to obtain a representation of average daily flow. [2]

If no historical or actual process wastewater flow data exist, the permitting authority is advised to establish a reasonable estimate of the facility's projected flow that is expected to be representative during the entire term of the permit. If a plant is planning significant production changes during the effective period of the permit, the permitting authority may consider establishing multiple tiers of limitations as a function of these production changes. Alternatively, a permit may be modified during its term, either at the request of the permittee or another interested party, or on EPA's initiative, to increase or decrease the flow basis in response to a significant change in production (40 CFR 124.5, 122.62). A change in production may be an "alteration" of the permitted activity or "new information" that could provide the basis for a permit modification (40 CFR 122.62(a)).

After determining the facility's annual average process wastewater flow, the permit writer would use this flow to convert the concentration-based limitations into mass-based limitations for ammonia and organic constituents for control at the end-of-pipe. The following example shows how a permit writer would establish daily maximum limits for a facility that generates wastewater from Subcategory B and C operations. The hypothetical facility's average daily wastewater generation (gal/day), the constituents in each stream, and the concentrations (mg/L) of each constituent are shown below.

Wastestream	Wastewater Source	Flow (gal/day)	Pollutants	Concentration (mg/L)
1	Subcategory B Process Flow	2,000	Methanol	250
2	Subcategory C Process Flow	30,000	Methanol tert-Butyl Alcohol Chlorobenzene	500 100 2
3	Noncontact Cooling Water	10,000	None	--

To estimate process wastewater discharge flow, the permit writer should review the component flows listed above and determine which wastewater flows can be deemed process wastewater discharge. In this example, only Subcategory B and C wastewater discharges constitute process wastewater discharge flow. Thus, a reasonable estimate of the process wastewater discharge flow for this example facility is 32,000 gal/day.

The limitations for chlorobenzene, methanol, and tert-butyl alcohol would be applied to the final effluent. The proposed Subcategory B and Subcategory C maximum daily limitations for chlorobenzene are both ND. Therefore, the permit limitation for chlorobenzene would be concentration-based and would be ND for all measurements. While the maximum daily limitation for methanol is ND for Subcategory C, the proposed limitation for Subcategory B is 6.60 μg/L. A limitation for the combined effluent would be calculated by using a numerical value equal to the minimum level for the Subcategory C wastewater. This calculation is shown in the example below.

The concentration-based limitations for methanol and tert-butyl alcohol would be converted to mass-based limitations using the annual average daily process wastewater discharge flow, 32,000 gal/day. This conversion can be calculated using the following equation:

$$L_M = L_C \times F \times k \qquad (15\text{-}1)$$

where:

L_M = mass-based effluent limitation, lbs/day
L_C = concentration-based effluent limitation, mg/L
F = average process wastewater discharge, gal/day
k = unit conversion factor, (L $\times$ lbs)/(gal $\times$ mg).

For this example, the unit conversion factor, k, is used to convert from [(mg/L) × (gal/day)] to (lbs/day) as follows:

$$k = (1\,L/0.264179\,gal) \times (1\,g/1000\,mg) \times (1\,lb/453.592\,g) = 8.345 \times 10^{-6}\ (L \times lbs)/(gal \times mg)$$

For this example, the mass-based maximum daily limitations for methanol and tert-butyl alcohol would be calculated using Equation 15-1:

Methanol:

Stream 1 L_M = (6.66 mg/L) × (2,000 gal/day) × 8.345×10^{-6} = 0.11 lbs/day

Stream 2 L_M = (3.18 mg/L) × (30,000 gal/day) × 8.345×10^{-6} = 0.80 lbs/da

Total L_M = 0.91 lbs/day methanol

Tert-butyl alcohol:

Stream 1 L_M = (3.98 mg/L) × (2,000 gal/day) × 8.345×10^{-6} = 0.07 lbs/day

Stream 2 L_M = (0.668 mg/L) × (30,000 gal/day) × 8.345×10^{-6} = 0.17 lbs/d

Total L_M = 0.24 lbs/day tert-butylalcohol

Thus, the maximum daily limitations for methanol and tert-butyl alcohol would be 0.91 lbs/day and 0.24 lbs/day, respectively. The monthly average limitations would be calculated in a similar manner and are shown below.

Methanol:

Stream 1 L_M = (3.18 mg/L) × (2,000 gal/day) × 8.345×10^{-6} = 0.05 lbs/day

Stream 2 L_M = (3.18 mg/L) × (30,000 gal/day) × 8.345×10^{-6} = 0.80 lbs/day

Total L_M = 0.85 lbs/day methanol

Tert-butyl alcohol:

Stream 1 L_M = (1.69 mg/L) × (2,000 gal/day) × 8.345×10^{-6} = 0.03 lbs/day

Stream 2 L_M = (0.284 mg/L) × (30,000 gal/day) × 8.345×10^{-6} = 0.07 lbs/day

Total L_M = 0.10 lbs/day tert-butylalcohol

The monthly average limitations for methanol and tert-butyl alcohol would be 0.85 lbs/day and 0.10 lbs/day, respectively.

There are no mass allowances for noncontact cooling water. Additional detailed guidance on the establishment of permit limitations is available in the Guidance for Implementing the Pharmaceutical Manufacturing Industry Regulations, included as Appendix A.

15.3.4 Monitoring and Compliance

Compliance monitoring for ammonia and all regulated organic constituents should be performed weekly. The list of pollutants for which monitoring would be required includes all regulated constituents listed in Table 15-1 generated or used in pharmaceutical manufacturing processes at the facility. Based on the proposed limitations, monitoring of ammonia and organic constituents generated or used in pharmaceutical manufacturing processes would occur prior to discharge to waters of the United States. Monitoring for cyanide based on the proposed cyanide limitations would be performed prior to commingling or dilution with non-cyanide bearing wastewater.

Monitoring should be conducted at a minimum of once for every treated batch of cyanide-bearing wastewater from Subcategory A and C process operations.

Compliance with the proposed effluent limitations guidelines for cyanide, if finalized, should be determined by comparing the concentration of cyanide with the daily maximum concentration-based limitation listed in Table 15-2. The monthly average concentration should be calculated by averaging the available measurements taken in each calendar month. Concentrations equal to or less than the concentrations listed in Table 15-2 would be in compliance.

Compliance with mass-based permit limitations for pollutants monitored prior to discharge to waters of the United States should be determined by multiplying the measured concentration of a regulated pollutant in the effluent sample by a conversion factor and the total wastewater flow at the monitoring location during the effluent sampling period, which is typically 24 hours. Thus, the mass compliance value should be based on the total flow discharged on the day of sampling, not on the long-term average process water flow rate that provided the basis for establishing the permit limitations and standards. The mass compliance value can be determined using the following equation:

$$CV_M = P_C \times F \times k \qquad (15\text{-}2)$$

where:

CV_M	=	mass compliance value, lbs/day
P_C	=	pollutant concentration, mg/L
F	=	total wastewater discharge flow through the monitoring point over 24-hour sampling period, gal/day
k	=	unit conversion factor, 8.345×10^{-6} (L × lbs)/(gal × mg).

For example, if analytical data from a 24-hour sampling period for a particular plant demonstrates a pollutant concentration of 5.0 mg/L, and the measured flow discharged through the monitoring point for the same 24-hour period is 0.600 million gallons, then

the plant's reported daily mass compliance value of the pollutant, using Equation 15-2, is 25.0 lbs/day. Similarly, the monthly average compliance value would be calculated by averaging the available daily mass compliance values in each calendar month.

For pollutants where the permit limitations are non-detect values, compliance is demonstrated by having all concentration-based measurements be below the minimum level that can be reliably measured by the analytical method for the pollutant. Minimum levels for all pollutants proposed to be regulated in this rulemaking are specified in Table 18-7.

The list of pollutants for which monitoring would be required should be updated based on consideration of raw material and process changes throughout the facility and an annual scan for cyanide and all pollutants listed in Table 15-1. After promulgation of a final rule for this industry, the annual scan should be performed at the compliance monitoring point(s) to identify any regulated pollutants in the wastewater. Permit monitoring and compliance should be required at all monitoring locations for all pollutants detected at any locations.

Table 15-1

Pollutants Proposed to be Regulated Under BAT

Priority Pollutants	
Benzene	1,2-Dichloroethane
Chlorobenzene	Methylene chloride
Chloroform	Phenol
Chloromethane (Methyl chloride)	Toluene
o-Dichlorobenzene (1,2-Dichlorobenzene)	Cyanide (a)
Nonconventional Pollutants	
Acetone	Formaldehyde
Acetonitrile	Formamide
Ammonia (a)	Furfural
Amyl acetate	n-Heptane
Amyl alcohol	n-Hexane
Aniline	Isobutyraldehyde
2-Butanone (MEK)	Isopropanol
n-Butyl acetate	Isopropyl acetate
n-Butyl alcohol	Isopropyl ether
tert-Butyl alcohol	Methanol
Chemical Oxygen Demand (COD)	Methylamine
Cyclohexane	Methyl cellosolve
Diethylamine	Methyl formate
Diethyl ether	2-Methylpyridine
N,N-Dimethylacetamide	Methyl isobutyl ketone (MIBK)
Dimethylamine	Petroleum naphtha
N,N-Dimethylaniline	Polyethylene glycol 600
N,N-Dimethylformamide	n-Propanol
Dimethyl Sulfoxide	Pyridine
1,4-Dioxane	Tetrahydrofuran
Ethanol	Trichlorofluoromethane
Ethyl acetate	Triethylamine
Ethylene glycol	Xylenes

(a) Ammonia and cyanide are proposed to be regulated in Subcategories A and C only.

Table 15-2

Proposed BAT Effluent Limitations for Subcategory A and C Operations

Pollutant or Pollutant Property	Proposed BAT Effluent Limitations for In-Plant Monitoring Points	
	Maximum for any 1 day µg/L	Monthly Average µg/L
Cyanide	766	406

Pollutant or Pollutant Property	Proposed BAT Effluent Limitations for End-of-Pipe Monitoring Points	
	Maximum for any 1 day µg/L	Monthly Average µg/L
Acetone	ND (50)	ND (50)
Acetonitrile	ND (5,000)	ND (5,000)
Ammonia	4,850	3,230
n-Amyl Acetate	105	45
Amyl Alcohol	668	ND (500)
Aniline	10	10
Benzene	ND (10)	ND (10)
2-Butanone (MEK)	202	86
n-Butyl Acetate	87	37
n-Butyl Alcohol	ND (500)	ND (500)
tert-Butyl Alcohol	668	284
Chemical Oxygen Demand (COD)	1,100,000	628,000
Chlorobenzene	ND (10)	ND (10)
Chloroform	ND (10)	ND (10)
Chloromethane	ND (50)	ND (50)
Cyclohexane	ND(5)	ND(5)
o-Dichlorobenzene	ND (10)	ND (10)
1,2-Dichloroethane	100	35

Table 15-2

(Continued)

Pollutant or Pollutant Property	Proposed BAT Effluent Limitations for End-of-Pipe Monitoring Points	
	Maximum for any 1 day µg/L	Monthly Average µg/L
Diethylamine	ND (50,000)	ND (50,000)
Diethyl Ether	574	244
Dimethylamine	ND (50,000)	ND (50,000)
N,N-Dimethylacetamide	ND (50)	ND (50)
N,N-Dimethylaniline	50	50
N,N-Dimethylformamide	45	19
Dimethyl Sulfoxide	ND (20,000)	ND (20,000)
1,4-Dioxane	220	94
Ethanol	ND (3,180)	ND (3,180)
Ethyl Acetate	105	45
Ethylene Glycol	ND (100,000)	ND (100,000)
Formaldehyde	1,480	623
Formamide	ND (100,000)	ND (100,000)
Furfural	2,670	1,140
n-Heptane	ND (10)	ND (10)
n-Hexane	ND (10)	ND (10)
Isobutyraldehyde	1,370	581
Isopropanol	ND (200)	ND (200)
Isopropyl Acetate	87	37
Isopropyl Ether	574	244
Methanol	ND (3,180)	ND (3,180)
Methylamine	ND (50,000)	ND (50,000)
Methyl Cellosolve	ND (20,000)	ND (20,000)
Methyl Formate	105	ND (100)

Table 15-2

(Continued)

Pollutant or Pollutant Property	Proposed BAT Effluent Limitations for End-of-Pipe Monitoring Points	
	Maximum for any 1 day µg/L	Monthly Average µg/L
Methylene Chloride	ND (10)	ND (10)
MIBK	ND (10)	ND (10)
2-Methylpyridine	50	50
Petroleum Naphtha	ND (10)	ND (10)
Phenol	25	14
Polyethylene Glycol 600	4,870	2,070
n-Propanol	ND (3,180)	ND (3,180)
Pyridine	10	10
Tetrahydrofuran	910	264
Toluene	ND (10)	ND (10)
Trichlorofluoromethane	ND (10)	ND (10)
Triethylamine	ND (50,000)	ND (50,000)
Xylenes	ND (10)	ND (10)

ND - Non-detect - A concentration-based measurement reported below the minimum level that can be reliably measured by the analytical method for the pollutant. Minimum levels are presented in parentheses corresponding to an analytical method applicable to the respective pollutant.

Table 15-3

Proposed BAT Effluent Limitations for Subcategory B and D Operations

Pollutant or Pollutant Property	Proposed BAT Effluent Limitations for End-of-Pipe Monitoring Points	
	Maximum for any 1 day µg/L	Monthly Average µg/L
Acetone	413	178
Acetonitrile	ND (5,000)	ND (5,000)
n-Amyl Acetate	3,000	1,280
Amyl Alcohol	3,980	1,690
Aniline	10	10
Benzene	40	17
2-Butanone (MEK)	202	86
n-Butyl Acetate	500	500
n-Butyl Alcohol	ND (500)	ND (500)
tert-Butyl Alcohol	3,980	1,690
Chemical Oxygen Demand (COD)	145,000	59,900
Chlorobenzene	ND (10)	ND (10)
Chloroform	22	13
Chloromethane	206	87
Cyclohexane	ND (5)	ND (5)
o-Dichlorobenzene	ND (10)	ND (10)
1,2-Dichloroethane	438	152
Diethylamine	ND (50,000)	ND (50,000)
Diethyl Ether	4,870	2,070
N,N-Dimethylacetamide	ND (50)	ND (50)
Dimethylamine	ND (50,000)	ND (50,000)
N,N-Dimethylaniline	50	50
N,N-Dimethylformamide	45	19
Dimethyl Sulfoxide	ND (20,000)	ND (20,000)
1,4-Dioxane	220	94
Ethanol	ND (3,180)	ND (3,180)
Ethyl Acetate	3,000	1,280
Ethylene Glycol	ND (100,000)	ND (100,000)

Table 15-3

(Continued)

Pollutant or Pollutant Property	Proposed BAT Effluent Limitations for End-of-Pipe Monitoring Points	
	Maximum for any 1 day µg/L	Monthly Average µg/L
Formaldehyde	1,480	623
Formamide	ND (100,000)	ND (100,000)
Furfural	3,000	1,280
n-Heptane	ND (10)	ND (10)
n-Hexane	ND (10)	ND (10)
Isobutyraldehyde	1,370	581
Isopropanol	1,120	476
Isopropyl Acetate	500	500
Isopropyl Ether	4,870	2,070
Methanol	6,660	ND (3,180)
Methylamine	ND (50,000)	ND (50,000)
Methyl Cellosolve	ND (20,000)	ND (20,000)
Methylene Chloride	1,420	357
Methyl Formate	3,000	1,280
MIBK	119	51
2-Methylpyridine	50	50
Petroleum Naphtha	40	17
Phenol	25	14
Polyethylene Glycol 600	4,870	2,070
n-Propanol	3,980	ND (3,180)
Pyridine	10	10
Tetrahydrofuran	15,000	4,350
Toluene	40	17
Trichlorofluoromethane	599	322
Triethylamine	ND (50,000)	ND (50,000)
Xylenes	ND (10)	ND (10)

ND - Nondetect - A concentration-based measurement reported below the minimum level that can be reliably measured by the analytical method for the pollutant. Minimum levels are presented in parentheses corresponding to an analytical method applicable to the respective pollutant.

REFERENCES

1. U.S. EPA, Office of Water. Statistical Support Document for the Proposed Effluent Limitations Guidelines for the Pharmaceutical Manufacturing Industry. U.S. Environmental Protection Agency, Washington, D.C., February 10, 1995.

2. U.S. EPA, Office of Water. Training Manual for NPDES Permit Writers. EPA 833-B-93-003, U.S. Environmental Protection Agency, Washington, D.C., 1993.

SECTION 16

NEW SOURCE PERFORMANCE STANDARDS (NSPS)

16.1 Introduction

The basis for new source performance standards under Section 306 of the CWA is the best available demonstrated technology. Industry has the opportunity to design and install the best and most efficient process operations and wastewater treatment systems at new pharmaceutical manufacturing facilities. Accordingly, Congress directed EPA to consider the best demonstrated alternative processes, process changes, in-plant control measures, and end-of-pipe wastewater treatment technologies that reduce pollution to the maximum extent feasible. In response to that directive, and as with the development of options for the proposed BAT effluent limitations guidelines, EPA considered effluent reductions attainable by the most advanced treatment technologies at pharmaceutical manufacturing facilities.

NSPS establish quantitative limits on the direct discharge of conventional, priority, and nonconventional pollutants to waters of the United States. These standards are based upon the performance of specific advanced technologies, but do not specify which technologies must be used to achieve compliance. NSPS are applied to individual facilities through NPDES permits issued by EPA or authorized states under Section 402 of the CWA. Each facility then chooses its own approach to complying with its permit limitations.

NSPS apply to all new sources in the pharmaceutical manufacturing industry. The NPDES permit regulations define the term "new source" at 40 CFR 122.2 and 122.29. According to these regulations, to be "new", a source must:

- Be constructed at a site at which no other source is located;
- Totally replace the process or production equipment that causes the discharge of pollutants at an existing source; or
- Be a process substantially independent of an existing source at the same site, considering the extent of integration with the existing source and the extent to which the new source is engaged in the same general type of activity as the existing source.

The Agency has selected in-plant steam stripping with distillation and cyanide destruction followed by end-of-pipe advanced biological treatment (NSPS Option 1) as the technology basis for the proposed NSPS for Subcategories A and C. The performance level of the advanced biological treatment system component of NSPS for subcategories A and C reflects the one best performing advanced biological treatment system at a facility with both subcategory A and C operations. The Agency has selected in-plant steam stripping with distillation followed by end-of-pipe advanced biological treatment (NSPS Option 2) as the technology basis for the proposed NSPS for Subcategories B and D. The performance level of the advanced biological treatment system component of NSPS for Subcategories B and D is the one best performing advanced biological treatment system of a facility with Subcategory D operations. The rationale behind these selections is discussed in Section 11.

The following information is presented in this section:

- Section 16.2 reviews the subcategories and the pollutants proposed to be regulated by NSPS and presents the proposed NSPS; and
- Section 16.3 discusses NSPS implementation with regard to point of application, permit limitations, and monitoring and compliance issues.

16.2 Summary of the Proposed NSPS

16.2.1 Regulated Subcategories

Revised NSPS are proposed for Subcategories A, B, C, and D. As discussed in Section 4.3, Subcategories A, B, and C include wastewater discharges resulting from the manufacture of pharmaceuticals by fermentation, biological or natural extraction processes, and chemical synthesis processes, respectively. Subcategory D includes wastewater discharges resulting from mixing, compounding, and formulating of pharmaceutical products.

16.2.2 Regulated Pollutants

The proposed NSPS establish effluent limitations for the conventional, priority, and nonconventional pollutants listed in Table 16-1 for direct dischargers in Subcategories A, B, C, and D. In addition, the proposed NSPS establish effluent limitations for cyanide and ammonia for direct dischargers in Subcategories A and C.

16.2.3 NSPS

The proposed NSPS for each subcategory are based on a combination of long-term mean effluent values and variability factors that account for day-to-day variation in measured treated effluent concentrations. Long-term means, discussed in Section 8, are target values that a facility should achieve on a long-term, average basis. The variability factors, discussed in the Statistical Support Document [1], which is located in the Administrative Record for this rulemaking, represent the ratio of an elevated value that would be expected to occur only rarely to the long-term mean. The variability factors are also provided in Appendix C of this document for ease of reference. The purpose of the variability factor is to allow for variations in effluent concentrations that comprise the long-term mean. A facility that designs and operates its treatment system to achieve

a long-term mean on a consistent basis should be able to comply with the daily and monthly limitations in the course of normal operations.

Table 16-2 presents the proposed maximum daily and monthly average NSPS for in-plant and end-of-pipe monitoring points for Subcategory A, and C operations. Table 16-3 presents the proposed maximum daily and monthly average NSPS for end-of-pipe monitoring points for Subcategory B and D operations.

The proposed regulation for the pharmaceutical manufacturing industry presents analytical method minimum levels in Section 439.1 (g). These values apply to those limitations and standards set at ND. For ease of use, the tables presented in this section present the analytical method minimum level in parentheses for those limitations and standards set at ND.

The pH effluent limit, established in the 1976 Final Rule (41 FR 50676) to be the range of 6.0 to 9.0 standard units for all subcategories, is not being revised.

16.3 Implementation of NSPS

As noted in Section 7, EPA is not proposing but is considering use of Best Management Practices (BMPs) to reduce discharges from leaks and spills of process chemicals and materials. These materials include organic solvents (some of which are ignitable) that contribute to air emissions and to effluent discharges and of-specification products which may upset biological treatment systems. BMPs may offer the opportunity to reduce these discharges and air emissions while concurrently increasing utilization of consumable materials. Suggested details on BMPs being considered for the pharmaceutical manufacturing industry are presented in Appendix B.

16.3.1 Establishing List of Pollutants for Compliance Monitoring

If final new source performance standards are promulgated as proposed, permit limitations would be established and compliance monitoring required for each pollutant listed on Table 16-1 generated or used at a pharmaceutical manufacturing facility. Limitations and routine compliance monitoring would not be required for regulated pollutants not generated or used at a facility. A determination that regulated pollutants are not generated or used would be based on a review of all raw materials used and an assessment of all chemical processes used, considering resulting products and by-products. The determination that a regulated pollutant is not generated or used would need to be confirmed by annual chemical analyses of wastewater from each monitoring location. Such confirmation would be provided by an analytical measurement of a non-detect value.

16.3.2 Point of Application

The proposed NSPS for ammonia (applicable to Subcategories A and C) and organic pollutants listed in Tables 16-2 and Table 16-3 are end-of-pipe standards and would be applicable to the final effluent at the point of discharge to waters of the United States. EPA also is soliciting comments and data on whether limits for the 12 most strippable priority and non-conventional organic pollutants should be applied at an in-plant monitoring point (e.g., following steam stripping and prior to dilution with other process and non-process wastewaters not containing these pollutants in treatable quantities and prior to end-of-pipe biological treatment systems). The limits EPA would propose for this in-plant monitoring point are found in Table 2-8. The proposed NSPS for cyanide, presented in Table 16-2, are applicable to Subcategories A and C. Compliance monitoring for cyanide would occur in plant, prior to dilution or mixing with any non-cyanide-bearing wastewater. In-plant monitoring would be required to prevent compliance through dilution with non-cyanide-bearing wastewater.

16.3.3 Permit Limitations

If final new source performance standards are promulgated as proposed, permit limitations for cyanide at in-plant locations should be concentration-based, and would not be converted to a mass basis. The proposed concentration-based standards for cyanide are listed in Table 16-2. A concentration basis should be used because it offers a direct benchmark to assess whether the in-plant control technology is achieving the intended NSPS level. In-plant wastestreams that require control may be generated or treated on a variable, batch basis. In such a setting, mass-based permit limitations are difficult to establish accurately, and compliance is hindered because the permitted facility cannot make a direct measurement to determine if its control technology is performing at the required level. Concentration-based permit limitations eliminate these problems and offer a direct measure to both the permitting authority and the permitted facility that NSPS performance levels are being achieved.

Permit limitations for ammonia, conventional, and nonconventional organic pollutants that EPA proposed to control at end-of-pipe should be mass-based unless the maximum for any one day limitation is non-detect (ND). In such a case, the permit should specify that all measured values should be non-detect values. Non-detect values are concentration-based measurements reported below the minimum level that can be reliably measured by the analytical method for the pollutant. The minimum level is the level at which an analytical system gives recognizable signals and an acceptable calibration point. Minimum levels for all regulated pollutants are specified in Table 18.7.

Permit writers would use a reasonable estimate of process wastewater discharge flow and the concentration-based standards listed in Tables 16-2 and 16-3 to develop mass-based permit limitations for the NPDES permit. Section 15.3.3 presents guidance regarding how a reasonable estimate of process wastewater discharge flow would be established after final NSPS are adopted.

The following example shows how a permit writer would establish daily maximum limits for a facility with wastewaters from Subcategories B and C process operations. The hypothetical facility's average daily wastewater generation (gal/day), the pollutants in each stream, and the concentrations (mg/L) of each constituent are as follows:

Wastestream	Wastewater Source	Flow (gal/day)	Pollutants	Concentration (mg/L)
1	Subcategory B Process Flow	2,000	Methanol BOD COD TSS	250 2,100 3,000 250
2	Subcategory C Process Flow	30,000	Methanol Aniline BOD COD TSS	500 20 800 1,800 130
3	Noncontact Cooling Water	10,000	None	

To estimate process wastewater discharge flow, the permit writer should review the component flows listed above and determine which wastewater flows can be deemed process wastewater discharge. In this example, only Subcategory A and B wastewater discharges constitute process wastewater discharge flow. Thus, a reasonable estimate of the process wastewater discharge flow for this example facility is 32,000 gal/day.

All limitations would be applied to the final effluent. The concentration-based standards for methanol and aniline are listed in Tables 16-2 and 16-3 for subcategories C and B, respectively. Note that they are the same for both subcategories. The standards for aniline would be converted to mass-based permit limitations using the annual average

daily process wastewater discharge flow, 32,000 gal/day. This conversion can be calculated using the following equation:

$$L_M = L_C \times F \times k \qquad (16\text{-}1)$$

where:
- L_M = mass-based effluent limitation, lbs/day
- L_C = concentration-based effluent limitation, mg/L
- F = average process wastewater discharge, gal/day
- k = unit conversion factor, (L x lbs)/(gal x mg).

For this example, the unit conversion factor, k, is used to convert from [(mg/L) x (gal/day)] to (lbs/day):

$$k = (1\ L/0.264179\ gal) \times (1\ g/1000\ mg) \times (1\ lb/453.592\ g) = 8.345 \times 10^{-6}\ [(L \times lbs)/(gal \times mg)]$$

For this example, the mass-based maximum daily and monthly average limitations for aniline would be calculated using Equation 16-1:

Maximum daily:

$L_M = (0.010\ mg/L) \times (32{,}000\ gal/day) \times 8.345 \times 10^{-6}\ [(L \times lbs)/(gal \times mg)]$
$L_M = 0.0027$ lbs/day aniline

Monthly average:

$L_M = (0.004\ mg/L) \times (32{,}000\ gal/day) \times 8.345 \times 10^{-6}\ [(L \times lbs)/(gal \times mg)]$
$L_M = 0.0011$ lbs/day aniline

The Subcategory B and the Subcategory C maximum daily limitations for methanol are ND. Therefore, the permit limitation for methanol should be ND for all measurements.

The proposed NSPS for BOD_5, COD, and TSS would also be applied to the final effluent at the point of discharge to waters of the United States. An example calculation of permit limitations for BOD_5 follows. The concentration-based standards for BOD_5 would also be converted to mass-based permit limitations using Equation 16-1. However, the concentration-based effluent limitation, L_C, for BOD_5 would be determined from the different limitations set for Subcategory B (from Table 16-3) and Subcategory C (from Table 16-2) wastewaters using the following equation:

$$L_C = \frac{(L_B \times F_B) + (L_C \times F_C)}{F_{B+C}} \qquad (16\text{-}2)$$

where:

L_C = combined concentration-based effluent limitations, (mg/L)

L_B = concentration-based effluent limitation for Subcategory B wastewater, mg/L

L_C = concentration-based effluent limitation for Subcategory C wastewater, mg/L

F_B = flow of Subcategory B wastewater, gal/day

F_C = flow of Subcategory C wastewater, gal/day

F_{B+C} = flow of Subcategory B wastewater and Subcategory C wastewater, gal/day.

For this example, the mass-based maximum daily limitation for BOD_5 would be calculated using Equations 16-1 and 16-2:

$$BOD_5\text{: } L_M = \left[\frac{(34\ mg/L \times 2{,}000\ gal/day) + (62\ mg/L \times 30{,}000\ gal/day)}{32{,}000\ gal/day}\right] \times (32{,}000\ gal/day) \times (8.345 \times 10^{-6})$$

$$L_M = 16\ lbs/day\ BOD_5$$

There are no mass allowances for noncontact cooling water. The monthly average permit limitation for BOD_5, and limitations for COD and TSS would be calculated in a

similar manner. Additional detailed guidance on establishing permit limitations is available in the Guidance for Implementing the Pharmaceutical Manufacturing Industry Regulations included as Appendix A.

16.3.4 Monitoring and Compliance

Compliance monitoring for the proposed NSPS for BOD_5, COD, TSS, and pH, if finalized, should be performed daily. Similarly, compliance monitoring for ammonia (for subcategories A and C) and all regulated organic constituents, based on final NSPS, in wastewater should be performed weekly. The list of pollutants for which EPA proposes to require monitoring includes all regulated constituents listed in Table 16-1 generated or used in pharmaceutical manufacturing processes at the facility. Under the proposed NSPS, monitoring for BOD_5, COD, TSS, pH, ammonia, and organic constituents generated or used in pharmaceutical manufacturing processes would occur at the point of discharge to waters of the United States. Similarly, monitoring for cyanide for Subcategories A and C would be performed prior to commingling or dilution with non-cyanide bearing wastewater. If final NSPS for cyanide are promulgated as proposed, monitoring should be conducted at a minimum of once for every treated batch of cyanide-bearing wastewater from Subcategory A and C process operations.

Compliance with the standards for cyanide, if promulgated as proposed, should be determined by comparing the concentration of cyanide with the daily maximum concentration-based limitation listed in Table 16-2. The monthly average concentration should be calculated by averaging the available measurements taken in each calendar month. Concentrations equal to or less than the concentrations listed in Table 16-2 would be in compliance.

Compliance with mass-based permit limitations for pollutants monitored prior to discharge to waters of the United States should be determined by multiplying the measured concentration of a regulated pollutant in the effluent sample by a conversion

factor and the total wastewater flow at the monitoring location during the effluent sampling period which is typically 24 hours. Thus, the mass compliance value should be based on the total flow discharged on the day of sampling, not on the long-term average process water flow rate that provided the basis for establishing the permit limitations and standards. The mass compliance value can be determined using the following equation:

$$CV_M = P_C \times F \times k \qquad (16\text{-}3)$$

where:

CV_M = mass compliance value, lbs/day

P_C = pollutant concentration, mg/L

F = total wastewater discharge flow through the monitoring point over 24-hour sampling period, gal/day

k = unit conversion factor, 8.345×10^{-6}.

For example, if analytical data from a 24-hour sampling period for a particular plant demonstrates a pollutant concentration of 5.0 mg/L, and the measured flow discharged through the monitoring point for the same 24-hour period is 0.600 million gallons, then the plant's reported daily mass compliance value of the pollutant, using Equation 16-3, is 25.0 lbs/day. Similarly, the monthly average compliance value would be calculated by averaging the available daily mass compliance values in each calendar month.

For pollutants where the permit limitations are non-detect values, compliance would be demonstrated by having all concentration-based measurements be below the minimum level that can be reliably measured by the analytical method for the pollutant. Minimum levels for all regulated pollutants are specified in Table 18-7.

The list of pollutants for which EPA proposes to require monitoring should be updated based on consideration of raw material and process changes throughout the facility and an annual scan for cyanide and all regulated pollutants in Table 16-1. The annual scan

should be performed at the compliance monitoring point(s) to identify any regulated pollutants in the wastewater. Permit monitoring and compliance should be required at all monitoring locations for all pollutants detected at any locations.

Table 16-1

Pollutants Proposed to be Regulated Under NSPS

Conventional Pollutants	
BOD_5	TSS
Priority Pollutants	
Benzene	1,2-Dichloroethane
Chlorobenzene	Methylene chloride
Chloroform	Phenol
Chloromethane (Methyl chloride)	Toluene
o-Dichlorobenzene (1,2-Dichlorobenzene)	Cyanide (a)
Nonconventional Pollutants	
Acetone	Formamide
Acetonitrile	Furfural
Ammonia (a)	n-Heptane
Amyl acetate	n-Hexane
Amyl alcohol	Isobutyraldehyde
Aniline	Isopropanol
2-Butanone (MEK)	Isopropyl acetate
n-Butyl acetate	Isopropyl ether
n-Butyl alcohol	Methanol
tert-Butyl alcohol	Methylamine
Cyclohexane	Methyl cellosolve
Diethylamine	Methyl formate
Diethyl ether	2-Methylpyridine
N,N-Dimethylacetamide	Methyl isobutyl ketone (MIBK)
Dimethylamine	Petroleum naphtha
N,N-Dimethylaniline	Polyethylene glycol 600
N,N-Dimethylformamide	n-Propanol
Dimethyl Sulfoxide	Pyridine

Table 16-1

(Continued)

Nonconventional Pollutants (cont.)	
1,4-Dioxane	Tetrahydrofuran
Ethanol	Trichlorofluoromethane
Ethyl acetate	Triethylamine
Ethylene glycol	Xylenes
Formaldehyde	COD (Chemical Oxygen Demand)

(a) Cyanide and ammonia are proposed to be regulated for Subcategories A and C only.

Table 16-2

Proposed NSPS for Subcategory A and C Operations

Pollutant or Pollutant Property	Proposed NSPS for In-Plant Monitoring Points	
	Maximum for any 1 day µg/L	Monthly Average µg/L
Cyanide	766	406

Pollutant or Pollutant Property	Proposed NSPS for End-of-Pipe Monitoring Points	
	Maximum for any 1 day µg/L	Monthly Average µg/L
Acetone	ND (50)	ND (50)
Acetonitrile	ND (5,000)	ND (5,000)
Ammonia	4,850	3,230
Amyl Alcohol	ND (500)	ND (500)
n-Amyl Acetate	14	6
Aniline	10	4
Benzene	ND (10)	ND (10)
2-Butanone (MEK)	144	61
n-Butyl Acetate	11	ND (5)
n-Butyl Alcohol	ND (500)	ND (500)
tert-Butyl Alcohol	ND (100)	ND (100)
Chlorobenzene	ND (10)	ND (10)
Chloroform	ND (10)	ND (10)
Chloromethane	ND (50)	ND (50)
Cyclohexane	ND (5)	ND (5)
o-Dichlorobenzene	ND (10)	ND (10)
1,2-Dichloroethane	13	ND (10)
Diethylamine	ND (50,000)	ND (50,000)
Diethyl Ether	74	ND (50)
N,N-Dimethylacetamide	ND (50)	ND (50)
Dimethylamine	ND (50,000)	ND (50,000)
N,N-Dimethylaniline	50	45
N,N-Dimethylformamide	45	19
Dimethyl Sulfoxide	ND (20,000)	ND (20,000)
1,4-Dioxane	ND (50)	ND (50)
Ethanol	ND (3,180)	ND (3,180)
Ethyl Acetate	14	ND (10)
Ethylene Glycol	ND (100,000)	ND (100,000)

Table 16-2

(Continued)

Pollutant or Pollutant Property	Proposed NSPS for End-of-Pipe Monitoring Points	
	Maximum for any 1 day μg/L	Monthly Average μg/L
Formaldehyde	1,480	623
Formamide	ND (100,000)	ND (100,000)
Furfural	53	ND (50)
n-Heptane	ND (10)	ND (10)
n-Hexane	ND (10)	ND (10)
Isobutyraldehyde	304	129
Isopropanol	ND (200)	ND (200)
Isopropyl Acetate	11	ND (10)
Isopropyl Ether	74	32
MIBK	ND (10)	ND (10)
Methanol	ND (3,180)	ND (3,180)
Methylamine	ND (50,000)	ND (50,000)
Methyl Cellosolve	ND (20,000)	ND (20,000)
Methylene Chloride	ND (10)	ND (10)
Methyl Formate	ND (100)	ND (100)
2-Methylpyridine	50	45
Petroleum Naphtha	ND (10)	ND (10)
Phenol	25	14
Polyethylene Glycol 600	4,870	2,070
n-Propanol	ND (3,180)	ND (3,180)
Pyridine	10	10
Tetrahydrofuran	910	264
Toluene	ND (10)	ND (10)
Trichlorofluoromethane	ND (10)	ND (10)
Triethylamine	ND (50,000)	ND (50,000)
Xylenes	ND (10)	ND (10)
BOD_5 (mg/L)	62	29
COD (mg/L)	781	538
TSS (mg/L)	87	43

ND - Nondetect - A concentration-based measurement reported below the minimum level that can be reliably measured by the analytical method for the pollutant. Minimum levels are presented in parentheses corresponding to an analytical method applicable to the respective pollutant.

Table 16-3

Proposed NSPS for Subcategory B and D Operations

Pollutant or Pollutant Property	Proposed NSPS for End-of-Pipe Monitoring Points	
	Maximum for any 1 day µg/L	Monthly Average µg/L
Acetone	ND (50)	ND (50)
Acetonitrile	ND (5,000)	ND (5,000)
n-Amyl Acetate	14	6
Amyl Alcohol	ND (500)	ND (500)
Aniline	10	4
Benzene	ND (10)	ND (10)
2-Butanone (MEK)	144	61
n-Butyl Acetate	11	ND (5)
n-Butyl Alcohol	ND (500)	ND (500)
tert-Butyl Alcohol	ND (100)	ND (100)
Chlorobenzene	ND (10)	ND (10)
Chloroform	ND (10)	ND (10)
Chloromethane	ND (50)	ND (50)
Cyclohexane	ND (5)	ND (5)
o-Dichlorobenzene	ND (10)	ND (10)
1,2-Dichloroethane	13	ND (10)
Diethylamine	ND (50,000)	ND (50,000)
Diethyl Ether	74	ND (50)
N,N-Dimethylacetamide	ND (50)	ND (50)
N,N-Dimethylaniline	50	45
N,N-Dimethylformamide	45	19
Dimethylamine	ND (50,000)	ND (50,000)
Dimethyl Sulfoxide	ND (20,000)	ND (20,000)
1,4-Dioxane	ND (50)	ND (50)
Ethanol	ND (3,180)	ND (3,180)
Ethyl Acetate	14	ND (10)
Ethylene Glycol	ND (100,000)	ND (100,000)
Formaldehyde	1,480	623
Formamide	ND (100,000)	ND (100,000)
Furfural	53	ND (50)

Table 16-3

(Continued)

Pollutant or Pollutant Property	Proposed NSPS for End-of-Pipe Monitoring Points	
	Maximum for any 1 day µg/L	Monthly Average µg/L
n-Heptane	ND (10)	ND (10)
n-Hexane	ND (10)	ND (10)
Isobutyraldehyde	304	129
Isopropanol	ND (200)	ND (200)
Isopropyl Acetate	11	ND (10)
Isopropyl Ether	74	32
MIBK	ND (10)	ND (10)
Methanol	ND (3,180)	ND (3,180)
Methylamine	ND (50,000)	ND (50,000)
Methyl Cellosolve	ND (20,000)	ND (20,000)
Methyl Formate	ND (100)	ND (100)
Methylene Chloride	ND (10)	ND (10)
2-Methylpyridine	50	45
Petroleum Naphtha	ND (10)	ND (10)
Phenol	25	14
Polyethylene Glycol 600	4,870	2,070
n-Propanol	ND (3,180)	ND (3,180)
Pyridine	10	10
Tetrahydrofuran	910	264
Toluene	ND (10)	ND (10)
Trichlorofluoromethane	ND (10)	ND (10)
Triethylamine	ND (50,000)	ND (50,000)
Xylenes	ND (10)	ND (10)
BOD_5 (mg/L)	34	10
COD (mg/L)	60	24
TSS (mg/L)	40	12

ND - Nondetect - A concentration-based measurement reported below the minimum level that can be reliably measured by the analytical method for the pollutant. Minimum levels are presented in parentheses corresponding to an analytical method applicable to the respective pollutant.

REFERENCES

1. U.S. EPA, Office of Water. Statistical Support Document for the Proposed Effluent Limitations Guidelines for the Pharmaceutical Manufacturing Industry. U.S. Environmental Protection Agency, Washington, D.C., February 10, 1995.

SECTION 17

PRETREATMENT STANDARDS FOR EXISTING SOURCES (PSES) AND PRETREATMENT STANDARDS FOR NEW SOURCES (PSNS)

17.1 Introduction

Pretreatment standards for existing sources are designed to prevent the discharge of pollutants which pass through, interfere with, or are otherwise incompatible with the operation of POTWs. The CWA requires pretreatment for pollutants that pass through POTWs in amounts that would exceed direct discharge effluent limitations or limit POTW sludge management alternatives, including the beneficial use of sludges on agricultural lands. EPA also determines that there is pass-through of a pollutant if the pollutant exhibits significant volatilization prior to treatment by POTWs. Pretreatment standards are to be technology-based and analogous to the BAT for removal of priority and nonconventional pollutants.

Section 307(c) of the CWA requires EPA to promulgate pretreatment standards for new sources at the same time that it promulgates NSPS. New indirect discharging facilities, like new direct discharging facilities, have the opportunity to incorporate the best available demonstrated technologies, including process changes, in-plant control measures, and end-of-pipe wastewater treatment technologies that reduce pollution to the maximum extent feasible. Pretreatment standards for new sources (see Section 16 for a discussion of the definition of new source) are to be technology-based and analogous to the NSPS for the removal of priority and nonconventional pollutants.

The owners or operators of facilities subject to PSES or PSNS are not required to use the specific process technologies and wastewater treatment technologies selected by EPA to establish the PSES or PSNS, but may choose to use any combination of process

technologies and wastewater treatment to comply with permit limitations derived from the PSES or PSNS.

The Agency has selected in-plant steam stripping and cyanide destruction (PSES Option 1) as the technology basis for the proposed PSES for Subcategory A and C operations. The Agency has selected in-plant steam stripping (PSES Option 1) as the technology basis for the proposed PSES for Subcategory B and D operations. For PSNS, the Agency has selected in-plant steam stripping with distillation and cyanide destruction (PSNS Option 1) as the proposed technology basis for the proposed PSNS for Subcategory A and C operations. The Agency also selected in-plant steam stripping with distillation (PSNS Option 1) as the proposed PSNS for Subcategory B and D operations. The rationale behind these selections is discussed in Section 11.

The following information is presented in this section:

- Section 17.2 reviews the subcategories regulated by PSES and PSNS, the results of the Agency's POTW pass-through analysis to determine pollutants proposed to be regulated by PSES and PSNS, and presents the proposed PSES and PSNS; and
- Section 17.3 discusses PSES and PSNS implementation with regard to point of application, permit limitations, and monitoring and compliance issues.

17.2 Summary of the Proposed PSES and PSNS

17.2.1 Regulated Subcategories

Revised PSES and PSNS are proposed for Subcategories A, B, C, and D. As discussed in Section 4.3, Subcategories A, B, and C include wastewater discharges resulting from the manufacture of pharmaceuticals by fermentation, biological or natural extraction processes, and chemical synthesis processes, respectively. Subcategory D includes

discharges resulting from mixing, compounding, and formulating of pharmaceutical products.

17.2.2 POTW Pass-Through Analysis

Based on currently available data and information, the Agency evaluated POTW pass-through for those pollutants proposed for regulation as listed in Sections 6.6 and 6.7. In determining whether a pollutant is expected to pass through a POTW, the Agency assessed the following:

- Whether the pollutant would be volatilized from conveyance systems, equalization or other treatment units or POTW head works which are open to the atmosphere;
- Whether the nation-wide average percentage of a pollutant removed by well-operated POTWs achieving secondary treatment is less than the percentage removed by the BAT model treatment system; or
- Whether there are any specific instances of POTW interference, upset, or pass through known to the Agency as being caused by the pollutants proposed for regulation.

The uncontrolled transfer of a pollutant from water to air through volatilization does not constitute treatment. Therefore, the Agency has determined that those pollutants proposed for regulation that will undergo significant volatilization from conveyance systems, equalization, or other treatment units or POTW head works that are open to the atmosphere pass through POTWs and should be regulated by pretreatment standards. Pollutants with a Henry's Law constant equal to or greater than 2.7×10^{-6} atm/gmole/m^3 undergo significant volatilization and are considered to pass through POTWs for this reason. The list of organic pollutants that EPA has determined pass through POTWs based on this criteria are shown in Table 17-1.

The Agency also made a comparison of the nation-wide average percentage of a pollutant removed by well-operated POTWs achieving secondary treatment to the percentage removed by the BAT model treatment systems. Pollutants are considered to pass through POTWs if the average percentage removal by the BAT model treatment systems is greater than the average percentage removed by well-operated POTWS. The Agency evaluated the percentage removed by the BAT model treatment systems using the Detailed Questionnaire data submitted by direct dischargers and the long-term mean treatment performance concentrations developed for the BAT treatment technologies as discussed in Section 8. The major source of the nation-wide average percentage of a pollutant removed by well-operated POTWs achieving secondary treatment was the Domestic Sewage Study. (1) The list of organic pollutants that EPA has determined pass through POTWs based on this criteria are shown in Table 17-1.

The Agency has reviewed responses received from a pharmaceutical outreach questionnaire sent by EPA/EAD in February 1993 to selected POTWs whose wastewater influents include pharmaceutical facility sources. These responses were reviewed to identify pharmaceutical candidate pollutants that may be causing interference, upsets, or pass-through at POTWs. In addition, data collected by EPA from the Syracuse POTW and data submitted previously to EPA by the Syracuse POTW were also reviewed for evidence of pollutants that may cause POTW interference, upset, or pass through. Based on these reviews, POTW personnel have reported POTW interference or upset by discharges from pharmaceutical facilities of ammonia, tetrahydrofuran, and dimethyl sulfoxide.

EPA does not have sufficient data at this time to determine whether acetonitrile, polyethylene glycol 600, or COD pass through POTWs. Pending collection of additional data, EPA is not proposing pretreatment standards for acetonitrile, polyethylene glycol 600, or COD at this time. With regard to the priority pollutant cyanide, EPA found that this pollutant passes through POTWs because the removal of cyanide by the BAT cyanide destruction system is significantly greater than the documented removals by well-

operated POTWs achieving secondary treatment. Ammonia (aqueous) is also considered to pass through because most POTWs do not have nitrification capability that is part of the BAT model treatment system and therefore will not achieve as much ammonia removal as the BAT model treatment system. For a detailed discussion of the Agency's POTW pass-through analysis see the memorandum entitled, "POTW Pass-Through Analysis for the Pharmaceutical Manufacturing Industry" (2) which is located in the Record for this rulemaking.

Based on the pass through analysis, the Agency has arrived at two alternate determinations of POTW pass-through. The Agency is putting forward two proposals for PSES and PSNS based on these alternate pass-through determinations. Under co-proposal (1), based on the data and information currently available, EPA has determined that the 50 organic pollutants listed in Table 17-1 pass through POTWs. Under co-proposal (2), the Agency is considering a finding that 33 of the less volatile priority and nonconventional pollutants do not pass through. EPA has developed co-proposal (2) because of concerns expressed by industry representatives that EPA's pass-through analysis supporting co-proposal (1) may not be correct for some of the 33 less volatile priority and nonconventional pollutants.

17.2.3 Regulated Pollutants

Co-proposal (1) establishes PSES and PSNS standards for the priority and nonconventional pollutants listed in Table 17-2 for indirect dischargers in Subcategories A, B, C, and D. Co-proposal (2) establishes PSES and PSNS standards for the priority and nonconventional pollutants listed in Table 17-3 for indirect discharges in Subcategories A, B, C, and D.

The proposed regulation for the pharmaceutical manufacturing industry presents analytical method minimum levels in Section 439.1 (g). These values apply to those limitations and standards set at ND. For ease of use, the tables presented in this section

present the analytical method minimum level in parentheses for those limitations and standards set at ND.

There are five organic pollutants that were found to pass through POTWs that are not treatable by the proposed PSES technology basis of steam stripping or the PSNS technology basis of steam stripping with distillation. These pollutants are formaldehyde, N,N-dimethyl formamide, N,N-dimethyl acetamide, ethylene glycol, and dimethyl sulfoxide and EPA has not proposed pretreatment standards for them at this time. One technology which might serve as the basis for pretreatment of these five pollutants is package biological treatment of selected wastestreams. In the proposed rule, the Agency has solicited data on the performance of this technology or others for treating these five nonstrippable pollutants. Based on a review of any new treatment performance data collected or received by the Agency for these pollutants, EPA may develop pretreatment standards at a later date. PSES and PSNS for these five pollutants are currently reserved.

17.2.4 PSES and PSNS

The proposed PSES and PSNS for each subcategory are based on a combination of long-term mean treatment performance concentrations and variability factors that account for day-to-day variation in measured treated effluent concentrations. Long-term mean treatment performance concentrations, discussed in Section 8, are target values that a facility should achieve on a long-term, average basis. The variability factors, discussed in the Statistical Support Document (3), which is located in the Record for this rulemaking, represent the ratio of an elevated value that would be expected to occur only rarely to the long-term mean. The purpose of the variability factor is to allow for variations in effluent concentrations that comprise the long-term mean. Variability factors are provided in Appendix C for reference purposes. A facility that designs and operates its treatment system to achieve a long term mean on a consistent basis should

be able to comply with the daily and monthly limitations in the course of normal operations.

The proposed technology basis, and hence the proposed PSES, are the same for each of the four pharmaceutical manufacturing subcategories. The same is true for PSNS. The only difference between Subcategories A and C and Subcategories B and D is the absence of proposed ammonia and cyanide standards for Subcategories B and D. The proposed PSES under co-proposal (1) are presented in Table 17-4. The proposed PSES under co-proposal (2) are presented in Table 17-5. The proposed PSNS under co-proposal (1) are presented in Table 17-6. The proposed PSNS under co-proposal (2) are presented in Table 17-7. These proposed standards were determined by multiplying the long-term mean treatment performance concentrations for the selected treatment technology bases by the respective 1-day and 4-day variability factors (VFs).

17.3 Implementation of the PSES and PSNS

As noted in Section 7, EPA is not preparing but is considering use of Best Management Practices (BMPs) to reduce discharges from leaks and spills of process chemicals and materials. These materials include organic solvents (some of which are ignitable) that contribute to air emissions and to effluent discharges and off-speciation products which may upset biological treatment systems. BMPs may offer the opportunity to reduce these discharges and air emissions while concurrently increasing utilization of consumable materials. Suggested details on BMPs being considered for the pharmaceutical manufacturing industry are presented in Appendix B.

17.3.1 Establishing List of Pollutants for Compliance Monitoring

If final PSES and PSNS are adopted as proposed, permit limitations would be established and compliance monitoring required for each regulated pollutant listed on Table 17-2 or 17-3 generated or used at a pharmaceutical manufacturing facility

(depending upon which co-proposal is promulgated). Limitations and routine compliance monitoring would not be required for regulated pollutants not generated or used at a facility. A determination that regulated pollutants are not generated or used would be based on a review of all raw materials used and an assessment of all chemical processes used, considering resulting products and by-products. The determination that a regulated pollutant is not generated or used would need to be confirmed by annual chemical analyses of wastewater from each monitoring location. Such confirmation would be provided by an analytical measurement of a non-detect value.

17.3.2 Point of Application

PSES and PSNS under co-proposals (1) and (2) for wastewaters from Subcategory A, B, C, and D operations are applicable at both in-plant process area discharge points and at end-of-pipe discharge points, as denoted in Tables 17-4 through 17-7 depending upon the pollutant being regulated.

The in-plant monitoring points should be placed prior to dilution by nonprocess wastewater, commingling with other process wastestreams not containing the regulated pollutants at treatable levels, and any conveyance, equalization, or other treatment units which are open to the atmosphere. In-plant monitoring is required to prevent compliance through dilution by significant wastewater flows from other portions of the facility that do not contain these pollutants, and to prevent cross-media transfer of these pollutants from wastewater to the atmosphere during collection, equalization, and POTW biological treatment. The end-of-pipe monitoring point should be placed prior to discharge to the POTW sewer system.

The proposed PSES and PSNS for cyanide are applicable to those wastewaters from Subcategory A and C operations. Compliance monitoring for cyanide should occur in plant, prior to dilution or mixing with any noncyanide-bearing wastewater. EPA

proposes to require in-plant monitoring to prevent compliance through dilution with noncyanide-bearing wastewater.

17.3.3 Permit Limitations

If final PSES and PSNS are promulgated as proposed, EPA expects that permit limitations for cyanide and organic constituents at in-plant locations would be concentration-based, and not converted to a mass basis. Proposed concentration-based limitations are listed in Tables 17-4 and 17-5 for PSES, and Tables 17-6 and 17-7 for PSNS. A concentration basis should be used because it offers a direct benchmark to assess whether the in-plant control technology is achieving the intended PSES and PSNS levels. In-plant wastestreams that require control may be generated or treated on a variable, batch basis. In such a setting, mass-based permit limitations are difficult to establish accurately, and compliance is hindered because the permitted facility cannot make a direct measurement to determine if its control technology is performing at the required level. Concentration-based permit limitations eliminate these problems and offer a direct measure to both the permitting authority and the permitted facility that PSES and PSNS performance levels are being achieved.

Permit limitations for ammonia (for Subcategories A and C) and organic constituents that are controlled at the final effluent should be mass-based unless the maximum for any one day limitation is ND. In such a case the permit should specify that all measured values should be non-detect values.

Non-detect values are concentration-based measurements reported below the minimum level that can be reliably measured by the analytical method for the pollutant. The minimum level is the level at which an analytical system gives recognizable signals and an acceptable calibration point. Minimum levels for all pollutants proposed to be regulated are specified in Table 18-7.

If final PSES and PSNS are promulgated as proposed, permit writers would use a reasonable estimate of process wastewater discharge flow and the concentration-based standards listed in Tables 17-4 through 17-7 to develop mass-based permit limitations. Section 15.3.3 presents guidance regarding how a reasonable estimate of process wastewater discharge flow would be established after final PSES and PSNS are adopted.

The following example shows how a permit writer would establish daily maximum limits for a facility with wastewaters from Subcategory C and D process operations. The hypothetical facility's average daily wastewater generation (gal/day), the pollutants in each stream, and the concentrations (mg/L) of each constituent are as follows:

Wastestream	Wastewater Source	Flow (gal/day)	Pollutants	Concentration (mg/L)
1	Subcategory C Process Flow	20,000	Acetone Pyridine Toluene	50 2 5
2	Subcategory D Process Flow	8,000	Ethanol Toluene	100 2
3	Noncontact Cooling Water	5,000	None	--

To estimate process wastewater discharge flow, the permit writer should review the component flows listed above and determine which wastewater flows can be deemed process wastewater discharge. In this example, only Subcategory C and D wastewater discharges constitute process wastewater discharge flow. Thus, a reasonable estimate of the process wastewater discharge flow for this example facility is 28,000 gal/day.

Under co-proposal (1) for PSES, the limitation for toluene would be applied at in-plant locations, immediately following treatment of process wastewater streams 1 and 2, prior to any dilution, commingling with other process wastestreams not containing the regulated pollutants at treatable levels, and any conveyance, equalization, or other

treatment units which are open to the atmosphere. The maximum daily limitation for toluene is concentration-based, and is 0.198 mg/L (from Table 17-4). The monthly average limitation for toluene is 0.148 mg/L.

The limitations for acetone, ethanol, and pyridine under co-proposal (1) for PSES would be applied to the final effluent. The concentration-based limitations for these three pollutants would be converted to mass-based limitations using the annual average daily process wastewater discharge flow, 28,000 gal/day. This conversion can be calculated using the following equation:

$$L_M = L_C \times F \times K \qquad (17\text{-}1)$$

where:
- L_M = mass-based effluent limitation, lbs/day
- L_C = concentration-based effluent limitation, mg/L
- F = average process wastewater discharge, gal/day
- K = unit conversion factor, (L × lbs)/(gal × mg).

For this example, the unit conversion factor, k, is used to convert from [(mg/L) × (gal/day)] to (lbs/day) as follows:

$$K = (mg/L) \times \frac{1\ L}{0.264179\ gal} \times \frac{1\ g}{1{,}000\ mg} \times \frac{1\ lb}{453.592\ g} \times (gal/day) = 8.345 \times 10^{-6}$$

For this example, the mass-based maximum daily and monthly average limitations for acetone would be calculated using Equation 17-1:

Maximum daily limitation:

$$L_M = (31.4 \text{ mg/L}) \times (28{,}000 \text{ gal/day}) \times 8.345 \times 10^{-6} \left[\frac{\text{L} \times \text{lbs}}{\text{gal} \times \text{mg}} \right]$$

$$L_M = 7.34 \text{ lbs/day acetone}$$

Monthly average limitation:

$$L_M = (9.69 \text{ mg/L}) \times (28{,}000 \text{ gal/day}) \times 8.345 \times 10^{-6} \left[\frac{\text{L} \times \text{lbs}}{\text{gal} \times \text{mg}} \right]$$

$$L_M = 2.26 \text{ lbs/day acetone}$$

The limitations for ethanol and pyridine can be calculated in a similar manner.

Under co-proposal (2) for PSES, there would be no limitations for acetone, ethanol, and pyridine, but toluene would still have in-plant limitations. The limitations for toluene would be the same as those shown for co-proposal (1) for PSES.

Under co-proposal (1) for PSNS, the limitations for acetone, ethanol, and toluene would be applied at in-plant locations, immediately following treatment of wastewater streams 1 and 2, prior to any dilution, commingling with other process wastestreams not containing the regulated pollutants at treatable levels, and any conveyance, equalization, or other treatment units which are open to the atmosphere. The maximum daily limitations for acetone, ethanol, and toluene are concentration-based, and are 1.19 mg/L, 8.69 mg/L, and 0.184 mg/L, respectively. The monthly average limitations are 0.600 mg/L, 3.22 mg/L, and 0.135 mg/L, for acetone, ethanol, and toluene, respectively (from Table 17-6).

The limitations for pyridine under co-proposal (1) for PSNS would be applied to the final effluent. The concentration-based limitations for pyridine would be converted to

mass-based limitations using the annual average daily process wastewater discharge flow, 28,000 gal/day. This conversion can be calculated using Equation 17-1 as shown below:

Maximum daily limitation:

$$L_M = (1.00 \text{ mg/L}) \times (28{,}000 \text{ gal/day}) \times 8.345 \times 10^{-6} \left[\frac{\text{L} \times \text{lbs}}{\text{gal} \times \text{mg}}\right]$$

$$L_M = 0.23 \text{ lbs/day pyridine}$$

The monthly average limitation for pyridine would be the same as the maximum daily limitation, since the concentration standards for the maximum for any one day and the monthly average are the same.

Under co-proposal (2) for PSNS, there would be no limitations for acetone, ethanol, and pyridine, but toluene would still have in-plant limitations. The limitations for toluene would be the same as those shown for co-proposal (1) for PSNS.

There are no mass allowances for noncontact cooling water under PSES or PSNS. Additional detailed guidance on the establishment of permit limitations is available in the Guidance for Implementing the Pharmaceutical Manufacturing Industry Regulations, included as Appendix A.

17.3.4 Monitoring and Compliance

The list of pollutants for which monitoring would need to be performed includes all constituents from Subcategory A, B, C, and D operations listed in Table 17-2 or 17-3 generated or used by a facility's pharmaceutical manufacturing processes (depending upon which co-proposal is promulgated). Based on the proposed PSES and PSNS, monitoring of those constituents generated or used in any pharmaceutical manufacturing processes at the facility would occur at every in-plant control point. Compliance

monitoring for ammonia and all other regulated organic constituents would be performed at a minimum on a weekly basis. Monitoring for cyanide based on the proposed cyanide PSES and PSNS would be performed at a minimum of once for every treated batch of cyanide-bearing wastewater from Subcategory A and C process operations.

Compliance with the standards for pollutants regulated at in-plant locations, if promulgated as proposed, would be determined by comparing the concentrations of those regulated pollutants with the daily maximum concentration-based standards listed in Tables 17-4 through 17-7. The monthly average concentrations should be calculated by averaging the available 1-day concentration values in each calendar month. (Since EPA proposes to require weekly monitoring for nonconventional and priority organic pollutants, there should be a minimum of four values to average.) Concentrations equal to or less than the concentrations listed in Tables 17-4 through 17-7 for a particular pollutant would be in compliance.

Compliance with mass-based permit limitations applicable to the end-of-pipe effluent should be determined by multiplying the measured concentrations of a regulated pollutant in the effluent sample by a conversion factor and the total wastewater flow at the monitoring point during the effluent sampling period, which is typically 24 hours. Thus, the mass compliance value should be based on the total flow discharged on the day of sampling, not on the long-term average flow rate that provided the basis for establishing the permit limitations. The mass compliance value can be determined using the following equation:

$$CV_M = P_C \times F \times k \qquad (17\text{-}1)$$

where: CV_M = mass compliance value, lbs/day

P_C = pollutant concentration, mg/L

F = total wastewater discharge flow through the monitoring point over 24-hour sampling period, gal/day

k = unit conversion factor, 8.345×10^{-6}.

For example, if analytical data from a 24-hour sampling period for a particular plant demonstrates a pollutant concentration of 10.0 mg/L, and the measured flow discharged through the monitoring point for the same 24-hour period is 0.600 million gallons, then the plant's reported daily mass compliance value of the pollutant, using Equation 17-1, is 50.1 lbs/day. Similarly, the monthly average compliance value would be calculated by averaging the available daily mass compliance values in each calendar month.

For pollutants where the permit limitations are non-detect values, compliance would be demonstrated by having all concentration-based measurements be below the minimum level that can be reliably measured by the analytical method for the pollutant. Minimum levels for all pollutants proposed to be regulated are specified in Table 18-7.

The list of pollutants for which EPA proposes to require monitoring should be updated based on evaluation of raw material and process changes throughout the facility and an annual scan for all regulated pollutants in Table 17-2 or Table 17-3. The annual scan should be performed at all in-plant monitoring points, and at the facility end-of-pipe process wastewater discharge point, to identify any regulated pollutants in the wastewater. Permit monitoring and compliance should be required at all monitoring locations for all pollutants detected at any locations.

Table 17-1

Organic Pollutants Considered for Regulation That Pass Through POTWs

Pollutant	Passes Through Based on Volatilization Potential	Passes Through Based on Evaluation of % POTW Removal
Acetone	X	X
Acetonitrile		
n-Amyl acetate	X	X
Amyl alcohol	X	X
Aniline	X	X
Benzene	X	X
2-Butanone (MEK)	X	X
n-Butyl acetate	X	X
n-Butyl alcohol	X	X
tert-Butyl alcohol	X	X
Chlorobenzene	X	X
Chloroform	X	X
Chloromethane (Methyl chloride)	X	X
Cyclohexane	X	X
o-Dichlorobenzene (1,2-Dichlorobenzene)	X	X
1,2-Dichloroethane	X	X
Diethylamine	X	X
Diethyl ether	X	X
N,N-Dimethylacetamide		X
Dimethylamine	X	X
N,N-Dimethylaniline	X	X
N,N-Dimethylformamide		X
Dimethyl sulfoxide		X
1,4-Dioxane	X	X
Ethanol	X	X
Ethyl acetate	X	X

Table 17-1

(Continued)

Pollutant	Passes Through Based on Volatilization Potential	Passes Through Based on Evaluation of % POTW Removal
Ethylene glycol		X
Formaldehyde		X
Formamide	X	X
Furfural	X	X
n-Heptane	X	X
n-Hexane	X	X
Isobutyraldehyde	X	X
Isopropanol	X	X
Isopropyl acetate	X	X
Isopropyl ether	X	X
Methanol	X	X
Methylamine	X	X
Methyl cellosolve	X	
Methylene chloride	X	X
Methyl formate	X	X
Methyl isobutyl ketone (MIBK)	X	X
2-Methylpyridine	X	X
Petroleum naphtha	X	X
Phenol		
Polyethylene glycol 600		
n-Propanol	X	X
Pyridine	X	X
Tetrahydrofuran	X	X
Toluene	X	X
Trichlorofluoromethane	X	X
Triethylamine	X	X
Xylenes	X	X

Table 17-2

Pollutants Proposed to be Regulated Under PSES and PSNS Co-Proposal (1)

Priority Pollutants	
Benzene	1,2-Dichloroethane
Chlorobenzene	Methylene Chloride
Chloroform	Toluene
Chloromethane (Methyl chloride)	Cyanide (a)
o-Dichlorobenzene (1,2-Dichlorobenzene)	
Nonconventional Pollutants	
Acetone	n-Heptane
Ammonia (a)	n-Hexane
Amyl acetate	Isobutyraldehyde
Amyl alcohol	Isopropanol
Aniline	Isopropyl acetate
2-Butanone (MEK)	Isopropyl ether
n-Butyl acetate	Methanol
n-Butyl alcohol	Methylamine
tert-Butyl alcohol	Methyl cellosolve
Cyclohexane	Methyl formate
Diethylamine	2-Methylpyridine
Diethyl ether	Methyl isobutyl ketone (MIBK)
Dimethylamine	Petroleum naphtha
N,N-Dimethylaniline	n-Propanol
1,4-Dioxane	Pyridine
Ethanol	Tetrahydrofuran
Ethyl acetate	Trichlorofluoromethane
Formamide	Triethylamine
Furfural	Xylenes

(a) EPA proposes to regulate cyanide and ammonia for Subcategories A and C only.

Table 17-3

Pollutants Proposed to be Regulated Under PSES and PSNS Co-Proposal (2)

Pollutant	
Ammonia (a)	n-Heptane
Benzene	n-Hexane
Chlorobenzene	Methyl Cellosolve
Chloroform	Methylene Chloride
Chloromethane	Toluene
Cyanide (a)	Trichlorofluoromethane
Cyclohexane	Xylenes

(a) EPA proposes to regulate ammonia and cyanide for Subcategories A and C only.

Table 17-4

Proposed PSES for Subcategory A, B, C, and D Operations - Co-Proposal (1)

Pollutant or Pollutant Property	Proposed PSES for In-Plant Monitoring Points	
	Maximum for any 1 day µg/L	Monthly Average µg/L
Benzene	796	268
Chlorobenzene	796	268
Chloroform	ND (10)	ND (10)
Chloromethane	796	268
Cyanide (a)	766	406
Cyclohexane	796	268
n-Heptane	796	268
n-Hexane	796	268
Methyl Cellosolve	ND (20,000)	ND (20,000)
Methylene Chloride	809	279
Toluene	198	148
Trichlorofluoromethane	796	268
Xylenes	796	268

Pollutant or Pollutant Property	Proposed PSES for End-of-Pipe Monitoring Points	
	Maximum for any 1 day µg/L	Monthly Average µg/L
Acetone	31,400	9,690
Ammonia (a)	12,900	10,900
n-Amyl Acetate	23,900	8,050
Amyl Alcohol	607,000	205,000
Aniline	10,900,000	3,690,000
2-Butanone (MEK)	1,440,000	430,000
n-Butyl Acetate	23,900	8,050
n-Butyl Alcohol	10,900,000	3,690,000
tert-Butyl Alcohol	607,000	205,000
o-Dichlorobenzene	23,900	8,050

Table 17-4

(Continued)

Pollutant or Pollutant Property	Proposed PSES for End-of-Pipe Monitoring Points	
	Maximum for any 1 day µg/L	Monthly Average µg/L
1,2-Dichloroethane	23,900	8,050
Diethylamine	ND (50,000)	ND (50,000)
Diethyl Ether	23,900	8,050
Dimethylamine	607,000	205,000
N,N-Dimethylaniline	607,000	205,000
1,4-Dioxane	10,900,000	3,690,000
Ethanol	2,200,000	784,000
Ethyl Acetate	23,900	8,050
Formamide	607,000	205,000
Furfural	607,000	205,000
Isobutyraldehyde	23,900	8,050
Isopropanol	597,000	198,000
Isopropyl Acetate	23,900	8,050
Isopropyl Ether	23,900	8,050
Methanol	11,700,000	3,800,000
Methylamine	607,000	205,000
Methyl Formate	23,900	8,050
MIBK	23,900	8,050
2-Methylpyridine	607,000	205,000
Petroleum Naphtha	10,900,000	3,690,000
n-Propanol	2,790,000	941,000
Pyridine	1,000	1,000
Tetrahydrofuran	9,210	3,360
Triethylamine	ND (50,000)	ND (50,000)

ND - Nondetect - A concentration-based measurement reported below the minimum level that can be reliably measured by the analytical method for the pollutant. Minimum levels are presented in parentheses corresponding to an analytical method applicable to the respective pollutant.

(a) - EPA proposes to regulate cyanide and ammonia for Subcategories A and C only.

Table 17-5

Proposed PSES for Subcategory A, B, C, and D Operations - Co-Proposal (2)

Pollutant or Pollutant Property	Proposed PSES for In-Plant Monitoring Points	
	Maximum for any 1 day µg/L	Monthly Average µg/L
Benzene	796	268
Chlorobenzene	796	268
Chloroform	ND (10)	ND (10)
Chloromethane	796	268
Cyanide (a)	766	406
Cyclohexane	796	268
n-Heptane	796	268
n-Hexane	796	268
Methyl Cellosolve	ND (20,000)	ND (20,000)
Methylene Chloride	809	279
Toluene	198	148
Trichlorofluoromethane	796	268
Xylenes	796	268

Pollutant or Pollutant Property	Proposed PSES for End-of-Pipe Monitoring Points	
	Maximum for and 1 day µg/L	Monthly Average µg/L
Ammonia (a)	12,900	10,900

ND - Nondetect - A concentration-based measurement reported below the minimum level that can be reliably measured by the analytical method for the pollutant. Minimum levels are presented in parentheses corresponding to an analytical method applicable to the respective pollutant.

(a) - EPA proposes to regulate cyanide and ammonia for Subcategories A and C only.

Table 17-6

Proposed PSNS for Subcategory A, B, C, and D Operations - Co-Proposal (1)

Pollutant or Pollutant Property	Proposed PSNS for In-Plant Monitoring Points	
	Maximum for any 1 day µg/L	Monthly Average µg/L
Acetone	1,190	600
Amyl Alcohol	8,690	3,220
Benzene	573	212
n-Butyl Alcohol	8,690	3,220
tert-Butyl Alcohol	8,690	3,220
Chlorobenzene	573	212
Chloroform	ND (10)	ND (10)
Chloromethane	573	212
Cyanide (a)	766	406
Cyclohexane	573	212
Diethylamine	ND (50,000)	ND (50,000)
Diethyl Ether	2,230	826
Dimethylamine	ND (50,000)	ND (50,000)
Ethanol	8,690	3,220
Formamide	ND (100,000)	ND (100,000)
n-Heptane	573	212
n-Hexane	573	212
Isopropanol	8,690	3,220
Methanol	8,320	ND (3,180)
Methylamine	ND (50,000)	ND (50,000)
Methyl Cellosolve	ND (20,000)	ND (20,000)
Methylene Chloride	809	279
Methyl Formate	2,230	826
n-Propanol	8,690	3,220
Toluene	184	135
Trichlorofluoromethane	573	212
Triethylamine	ND (50,000)	ND (50,000)
Xylenes	573	212

Table 17-6

(Continued)

Pollutant or Pollutant Property	Proposed PSNS for End-of-Pipe Monitoring Points	
	Maximum for any 1 day μg/L	Monthly Average μg/L
Ammonia (a)	12,900	10,900
n-Amyl Acetate	2,230	826
Aniline	8,690	3,220
2-Butanone (MEK)	161,000	57,900
n-Butyl Acetate	2,230	826
o-Dichlorobenzene	2,230	826
1,2-Dichloroethane	2,230	826
N,N-Dimethylaniline	8,690	3,220
1,4-Dioxane	8,690	3,220
Ethyl Acetate	2,230	826
Furfural	8,690	3,220
Isobutyraldehyde	2,230	826
Isopropyl Acetate	2,230	826
Isopropyl Ether	2,230	826
MIBK	2,230	826
2-Methylpyridine	8,690	3,220
Petroleum Naphtha	8,690	3,220
Pyridine	1,000	1,000
Tetrahydrofuran	9,210	3,360

ND - Nondetect - A concentration-based measurement reported below the minimum level that can be reliably measured by the analytical method for the pollutant. Minimum levels are presented in parentheses corresponding to an analytical method applicable to the respective pollutant.

(a) - EPA proposes to regulate cyanide and ammonia for Subcategories A and C only.

Table 17-7

Proposed PSNS for Subcategory A, B, C, and D Operations - Co-Proposal (2)

Pollutant or Pollutant Property	Proposed PSNS for In-Plant Monitoring Points	
	Maximum for any 1 day μg/L	Monthly Average μg/L
Benzene	573	212
Chlorobenzene	573	212
Chloroform	ND (10)	ND (10)
Chloromethane	573	212
Cyanide (a)	766	406
Cyclohexane	573	212
n-Heptane	573	212
n-Hexane	573	212
Methyl Cellosolve	ND (20,000)	ND (20,000)
Methylene Chloride	809	279
Toluene	184	135
Trichlorofluoromethane	573	212
Xylenes	573	212

Pollutant or Pollutant Property	Proposed PSNS for End-of-Pipe Monitoring Points	
	Maximum for any 1 day μg/L	Monthly Average μg/L
Ammonia (a)	12,900	10,900

ND - Nondetect - A concentration-based measurement reported below the minimum level that can be reliably measured by the analytical method for the pollutant. Minimum levels are presented in parentheses corresponding to an analytical method applicable to the respective pollutant.

(a) - EPA proposes to regulate cyanide and ammonia for Subcategories A and C only.

REFERENCES

1. U.S. EPA, Office of Water Regulations and Standards. Report to Congress on the Discharge of Hazardous Wastes to Publicly Owned Treatment Works. U.S. Environmental Protection Agency, Washington, D.C., February 1986.

2. Memorandum: POTW Pass-Through Analysis for the Pharmaceutical Manufacturing Industry, from Mary Willett, Radian Corporation, to Frank Hund, U.S. EPA, October 1994.

3. U.S. EPA, Office of Water. Statistical Support Document for the Proposed Effluent Limitations Guidelines for the Pharmaceutical Manufacturing Industry. U.S. Environmental Protection Agency, Washington, D.C., February 10, 1995.

SECTION 18

ANALYTICAL METHODS

18.1 Regulatory Background

Section 304(h) of the Clean Water Act directs EPA to promulgate guidelines establishing test procedures (analytical methods) for analyzing pollutants. These test procedures are used for filing applications and for compliance monitoring under the National Pollutant Discharge Elimination System (NPDES) found at 40 CFR Parts 122.41(j)(4) and 122.21(g)(7), and for the pretreatment program found at 40 CFR 403.7(d). Promulgation of these methods is intended to standardize analytical methods within specific industrial categories and across industries.

EPA has promulgated analytical methods for monitoring pollutant discharges at 40 CFR Part 136, and has promulgated methods for analytes specific to given industrial categories at 40 CFR Parts 400 to 480. In addition to the methods developed by EPA and promulgated at 40 CFR Part 136, certain methods developed by others[1], have been incorporated by reference into 40 CFR Part 136. Methods not promulgated or incorporated by reference at 40 CFR Part 136 are being proposed for inclusion in 40 CFR Part 439 to support regulation of the discharges from the pharmaceutical manufacturing industry. For this proposed rule, EPA intends to regulate the conventional pollutants, BOD_5 and TSS; certain priority pollutants (toxic pollutants); and certain nonconventional pollutants that are not identified as priority pollutants or conventional pollutants as identified in Section 6. Table 18-1 lists the priority pollutants, conventional pollutants, and nonconventional pollutants proposed for regulation along with their Chemical Abstracts Service Registry Numbers (CASRNs).

[1]For example, the American Public Health Association publishes *Standard Methods for the Examination of Water and Wastewater.*

Section 18.2 describes the analytical methods used by EPA for gathering data on waste streams produced by the pharmaceutical manufacturing industry. Section 18.3 provides a description of the analytical methods proposed for compliance monitoring of pharmaceutical manufacturing industry wastewaters.

18.2 Analytical Methods Used By EPA For Data Gathering

The Agency acquired data on the presence and concentration of approximately 400 analytes during 18 sampling episodes and pilot studies conducted during a 10-year period from May of 1983 to October of 1993. The data collected during these studies and information acquired from the Detailed Questionnaire form the basis for regulation of the analytes listed in Table 18-1 and are used to establish the analytical methods and the effluent guidelines for these substances. In the following paragraphs, each method used for data gathering is described; promulgated methods will be referenced. Any modifications to the referenced methods for individual analytes are also described.

18.2.1 Conventional Pollutants and COD

Conventional pollutants and COD were determined using the EPA methods listed in 40 CFR Part 136.(1) Table 18-2 lists these methods.

18.2.2 Priority Pollutants

Table 18-3 lists the analytical methods used to determine the presence and concentration of the priority pollutants proposed for regulation. Methods 1624, 1625, 335.2, and 335.3 are promulgated methods (2) and are not further described here.

18.2.3 Nonconventional Pollutants

Table 18-4 lists the analytical methods used to determine the presence and concentration of the nonconventional pollutants proposed for regulation. Methods 1624, 1625, 8015 (3), and 350.2 (1) are promulgated methods and not further described here. Modification of a promulgated method is indicated in the "Notes" column; these method modifications are described in Sections 18.2.3.1 through 18.2.3.3. EPA did not perform analytical testing for 16 of the nonconventional pollutants listed in Table 18-4 (indicated by "No EPA Analysis" in the method column).

18.2.3.1 Methods 1624 and 1625; Reverse Search

Qualitative analysis of pollutants using gas chromatography/mass spectrometry (GC/MS) is performed in one of three ways. The primary method of identification uses an authentic standard. The GC/MS system is calibrated and the mass spectrum and retention time for each standard are stored in a user-created library. A pollutant is positively identified when its retention time and mass spectrum agree with the laboratory retention time and spectrum. The second method of qualitative analysis, reverse search, can be used when authentic standards are not available and the pollutant was not identified by the method described above. The unknown pollutant is considered identified if its retention time and mass spectrum agree with those specified in the method. The third method of qualitative analysis produces a list of analytes called "tentatively identified compounds (TICs)." For chromatographic peaks that have not been identified by comparison to an authentic standard and for which reverse search is unsuccessful, the background corrected spectrum at the peak maximum is compared with spectra in the NIST[2]/EPA/NIH Mass Spectral File.(4) Tentative identification is established when the spectrum agrees with one from this file.

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[2] National Institute of Standards and Technology.

Quantitative analysis of pollutants using GC/MS is performed in one of four ways using the extracted ion current profile (EICP) areas. The preferred method of quantitation is applicable to pollutants for which authentic standards and labeled analogs are available. (A labeled analog is a compound in which one or more of the constituent atoms has been replaced with a stable isotope such as deuterium or carbon-13.) In this method, the GC/MS system is calibrated and the analyte concentration is determined using an isotope dilution technique. A second method can be used when authentic standards are available, but labeled analogs are not. In this case, the GC/MS instrument is calibrated and the pollutant concentration is determined by using an internal standard technique. For reverse search pollutants, compound concentrations are determined by using known response factors. For TICs, pollutant concentration is determined using the sum of the EICP areas relative to the sum of the EICP areas of the nearest eluted internal standard.

18.2.3.2 Method 1624; Hot Purge

Analyses were performed as specified in Method 1624 with the following exception. If the solids content of the sample was known or determined to be less than one percent, stable isotopically labeled analogs of the compounds of interest were added to a five-milliliter sample and the sample was purged with an inert gas at 40°C in a chamber designed for water samples. If the solids content was greater than one percent, five milliliters of reagent water and the labeled analogs were added to a five-gram aliquot and the mixture was purged at 40°C in a chamber designed for soil or water samples. In the purging process, the volatile compounds are transferred from the aqueous phase into the gaseous phase and trapped on a sorbent column. After purging is completed, the trap is back flushed and rapidly heated to desorb the compounds for GC/MS analysis.

18.2.3.3 Method 8015[3]; Hot Purge

Analyses were performed as specified in Method 8015 using the purge and trap sample introduction (Method 5030) with the following exception. An inert gas was bubbled through the solution at 40°C, instead of the temperature specified in Method 8015, and the volatile components were transferred from the aqueous phase to the vapor phase. The vapor was swept through a sorbent column where the volatile components were trapped. After purging was completed, the sorbent column was heated and backflushed with inert gas to desorb the volatile components onto the chromatographic column.

18.3 Methods Proposed For Monitoring

Promulgated methods exist for all of the conventional pollutants and the priority pollutants. Seven nonconventional pollutants (COD, ammonium hydroxide (ammonia as N), acetone, 2-butanone, diethylether, p-dioxane, and α-picoline) have promulgated analytical methods. The Agency will require the use of these promulgated methods, newly developed Method 1665 for α-picoline, or equivalent methods[4], for purposes of compliance monitoring by the pharmaceutical manufacturing industry. Table 18-5 lists these pollutants and the promulgated analytical methods.

EPA has developed analytical procedures for all of the nonconventional pollutants that do not have methods published in 40 CFR Part 136. Two nonconventional pollutants that were considered for regulation for which analytical methods have not been developed are bis(chloromethyl)ether and dimethylcarbamyl chloride. These substances are rapidly hydrolyzed in aqueous solution and therefore cannot be detected in

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[3] Neither Method 8015 nor other SW-846 methods are promulgated at 40 CFR 136 for NPDES compliance monitoring purposes. Method 8015 was used in this initial screening of the pharmaceutical manufacturing industry.

[4] Alternate and equivalent test procedures are defined in 40 *CFR* 136.3(a), 136.4, and 136.5; in the preamble to promulgation of the 40 *CFR* 136, Appendix A methods (49 FR 43234); and in the text of the 40 *CFR* 136 Appendix A methods.

wastewater analyses. The Agency is, therefore, not proposing these pollutants for regulation but will monitor concentrations of their hydrolysis products (formaldehyde (5) and dimethylamine (6), respectively). The half-life for bis(chloromethyl)ether in water has been reported as 10-38 seconds.(7)

Table 18-6 lists those pollutants for which new analytical methods have been developed and provides a reference to those methods.(8) The pharmaceutical manufacturing industry will be allowed to use these methods for compliance monitoring.

18.3.1 Methods Development for Monitoring of Pharmaceutical Manufacturing Industry Effluents

Many of the non-conventional pollutants that may be released from the pharmaceutical manufacturing industry are not included in methods previously promulgated for monitoring effluents from other industries. For this reason it has been necessary to develop methods for these pollutants. Many of the pharmaceutical manufacturing industry effluents present difficult analytical challenges. Some are amenable to extraction from aqueous solution and can be analyzed by GC/MS after extraction and concentration. Method 1665 has been developed for these analytes. Others may be concentrated by purging from aqueous solution and trapping in a column containing sorbent material. For these substances, purge-and-trap followed by GC/MS analysis as described in Method 1666 was developed. Some highly water soluble pharmaceutical manufacturing industry analytes, however, cannot be extracted from aqueous solution and cannot be efficiently purged from water. For this reason, it was necessary to develop a direct aqueous injection gas chromatography (GC) option for Method 1666. in some cases, a GC with a flame ionization detector (GC/FID) provides better performance than GC/MS for the non-purgeable, water soluble analytes. Method 1671, using GC/FID was developed for these analytes. Formaldehyde is not extractable from water and cannot be readily analyzed by either purge-and-trap GC/MS or direct aqueous injection. For this reason a separate approach, Method 1667 utilizing derivatization

followed by high pressure liquid chromatography (HPLC), was developed for formaldehyde and the other aldehydes included in the pharmaceutical manufacturing industry analyte list. Poly(ethylene glycol)-600 (PEG-600) is a mixture of ethylene glycol oligomers with a molecular weight centered around 600 Da. GC/MS analysis was attempted for this pollutant without success. At 200 parts-per-million (ppm), under conditions used for Method 1665, constituents of PEG-600 were not detected. At 2000 ppm constituents of PEG-600 were detected by the GC/MS system, but with an extremely low response that was not suitable for quantitation. At higher concentrations, damage to the analytical system is likely. For these reasons, Method 1673, a derivatization/HPLC method, was developed for PEG-600. Methods 1665, 1666, 1667, 1671 and 1673 are briefly described below. A complete description of the methods can be found in the Methods Compendium.(8)

18.3.1.1 Method 1665

Method 1665 entitled "Semi-Volatile Organic Compounds Specific to the Pharmaceutical Manufacturing Industry by Isotope Dilution GC/MS" is proposed for compliance monitoring by the pharmaceutical manufacturing industry. The method is based upon Method 1625, Revision C.

Using Method 1665 the percent solids content of a sample is determined and stable isotopically labeled analogs of the compounds of interest are added to the sample. If the solids content of the sample is less than one percent, a one liter sample is extracted at pH 12-13 with methylene chloride using continuous extraction techniques. If the solids content is greater than one percent but less than 30 percent, the sample is diluted to one percent solids with reagent water, ultrasonically homogenized, and extracted as described for a sample with less than one percent solids. If the solids content is greater than 30 percent, the sample is extracted using ultrasonic techniques.

Each extract is dried over anhydrous sodium sulfate, concentrated to a volume of five milliliters, cleaned up using gel permeation chromatography (GPC), if necessary, and concentrated. Extracts are concentrated to one milliliter if GPC is not performed, and to 0.5 milliliter if GPC is performed. An internal standard is added to the extract, and an aliquot of the extract is injected into the gas chromatograph. The compounds are separated on the GC and detected by a mass spectrometer.

Analyte concentrations for substances with labeled analogs are determined by comparison of the extracted ion current profile (EICP) areas with those of the labeled analogs. Concentrations of analytes without labeled analogs are determined by comparison of EICP areas with an internal standard.

18.3.1.2 Method 1666

Method 1666 entitled "Volatile Organic Compounds Specific to the Pharmaceutical Manufacturing Industry by Isotope Dilution GC/MS" is proposed for compliance monitoring by the pharmaceutical manufacturing industry. The method is based, in part, upon Method 1624, Revision C. The method description is separated into two parts; the first part describes the purge-and-trap technique, and the second part describes direct aqueous injection.

Method 1666 - Purge-and-Trap

The percent solids content of the sample is determined. If the solids content is known or determined to be less than 1 percent, stable isotopically labeled analogs of the compounds of interest are added to a 5-milliliter (mL) sample and the sample is purged with an inert gas at 45 degrees celsius in a chamber designed for soil or water samples. In the purging process, the volatile compounds are transferred from the aqueous phase into the gaseous phase where they are passed into a sorbent column and trapped. For higher solids samples, five grams of solid is weighed into the purging device and five mL

of reagent water and the stable isotopically labeled analogs are added before purging. After purging is completed, the trap is backflushed and heated rapidly to desorb the compounds into a gas chromatograph where they are separated and detected by a mass spectrometer. The labeled compounds serve to correct the variability of the analytical technique.

Method 1666 - Direct Aqueous Injection

The percent solids content of the sample is determined. If the solids content is known or determined to be less than 1 percent, stable isotopically labeled analogs of the compounds of interest are added to a sample. If the solids content of the sample is greater than one percent, five mL of reagent water and the labeled compounds are added to a 5-gram aliquot of sample. The mixture is sonicated in a centrifuge tube with little or no headspace for five minutes. During this period the native analytes and labeled analogs will equilibrate between the solid and aqueous phases. In some cases, additional sonification may be necessary to establish equilibrium.

If necessary, the low solids sample may be centrifuged for clarification. High solids samples will be centrifuged to provide a clear supernate. An aliquot of the aqueous solution (or supernate) is injected into the GC/MS system. The compounds are separated by the GC and detected by the mass spectrometer. The labeled compounds serve to correct the variability of the analytical technique.

18.3.1.3 Method 1667

Method 1667 entitled "Formaldehyde, Isobutyraldehyde, and Furfural by Derivatization and High Pressure Liquid Chromatography" is proposed for compliance monitoring by the pharmaceutical manufacturing industry. This method is based on draft Method 8315.(3)

For pharmaceutical manufacturing industry wastes comprised of solids or for aqueous wastes containing significant amounts of solid material, the aqueous phase, if any, is separated from the solid phase and stored for later analysis. If necessary, the particle size of the solids in the waste is reduced. Twenty-five grams of the solid phase is extracted with 500 milliliters of extraction fluid[5]. The extraction fluid employed is a function of the alkalinity of the solid phase of the waste. Following extraction, the aqueous extract is separated from the solid phase by filtration employing a glass fiber filter.

If compatible (i.e., multiple phases will not form on combination), the initial aqueous phase of the pharmaceutical manufacturing industry waste is added to the aqueous extract, and these liquids are analyzed together. If incompatible, the liquids are analyzed separately and the results are mathematically combined to yield a volume-weighted average concentration.

A measured volume of aqueous sample or an appropriate amount of solids leachate is buffered to pH = 5 and derivatized with 2,4-dinitrophenylhydrazine (DNPH), using either a solid sorbent or methylene chloride derivatization/extraction option. If the solid sorbent option is used, the derivative is extracted using solid sorbent cartridges, followed by elution with ethanol. If the methylene chloride option is used, the derivative is extracted with methylene chloride, the methylene chloride extracts are concentrated using the Kuderna-Danish procedure and solvent exchanged into methanol prior to high pressure liquid chromatographic analysis. Liquid chromatographic conditions are utilized that permit the separation and measurement of the derivatized pharmaceutical manufacturing industry analytes in the extract by absorbance detection at 365 nanometers.

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[5] A proportionally smaller amount of extraction fluid is used if less solid phase is available.

Quantitation of the pharmaceutical manufacturing industry analytes is performed by an external standard technique. Known concentrations of the pharmaceutical manufacturing industry analytes are carried through the derivatization/extraction procedure and peak areas at 365 nanometers measured. The peak areas of the standards are plotted against concentration of the original aldehydes and the samples quantified by comparison to the standards. Precision and accuracy of the procedure is assured by use of careful quality assurance and quality control techniques including analysis of initial precision and recovery standards and ongoing precision and accuracy samples. Matrix spike and matrix spike duplicate analyses are performed, when appropriate.

18.3.1.4 Method 1671

Method 1671 "Volatile Organic Compounds Specific to the Pharmaceutical Manufacturing Industry by GC/FID" is proposed for compliance monitoring by the pharmaceutical manufacturing industry. The method was developed because some of the non-purgeable, water-soluble pharmaceutical manufacturing industry analytes did not perform well in GC/MS investigations.

For aqueous samples, one or more internal standard is added to a 5 mL aliquot. If the solids content of the sample is known or determined to be greater than 1 percent, 5 mL of reagent water is added to a 5 gram sample along with the internal standard(s). This mixture is sonicated for five minutes in a centrifuge tube and the resulting equilibrated sample centrifuged. An appropriate amount of aqueous solution or supernate is injected into the GC/FID system. Identification is based on gas chromatographic retention time and quantitation is performed by an internal standard technique. Precision and accuracy of the Method is assured by use of careful quality assurance and quality control techniques including analysis of blanks, use of calibration solutions, and matrix spike and matrix spike duplicate analysis.

18.3.1.5 Method 1673

Method 1673 entitled "Poly(ethylene glycol)-600 by Derivatization and High Pressure Liquid Chromatography" is proposed for compliance monitoring by the pharmaceutical manufacturing industry. Derivatization of the PEG-600 polymeric mixture with a substance that absorbs in the ultraviolet (UV) provides increased sensitivity over other methods of determination and allows quantitation at one part-per-million.

This method has been developed for aqueous samples and is not, in its present form, applicable to solids or sludges. One liter of aqueous sample is placed into a liquid-liquid extractor and a known quantity of surrogate is added. Extraction with dichloromethane is carried out for an 18-hour period. The dichloromethane extracts are dried over anhydrous sodium sulfate, evaporated to a small volume and dried again. The water-free extract is derivatized using 3,5-dinitrobenzoyl chloride and pyridine. The derivatized extract is treated with water to hydrolyze excess derivatization reagent. The extract is diluted with diethyl ether (ether), washed with acid and base, and the ether evaporated. The remaining is solvent exchanged with acetonitrile/water and chromatographed on a reverse-phase C_{18} column with a solvent gradient of 40% acetonitrile/water to 100% acetonitrile. Detection is performed at 254 nanometers. The PEG-600 derivative is identified by its retention time relative to that of the surrogate and quantified by external standard techniques. Derivatized samples must be stored at 4°C in an amber container and analyzed within 96 hours of preparation.

Because PEG-600 is a mixture of poly(ethylene glycol) oligomers (polymers containing relatively few structural units), the exact nature of PEG-600 samples from various manufacturers and different batches from a single manufacturer may vary. For this reason, concentrations of PEG-600 in a specific waste stream are best determined when standards are prepared using the same batch of PEG-600 in use by the pharmaceutical manufacturer at the time of discharge to the waste stream under analysis. Where it is not possible to obtain a discharge-specific PEG-600 standard, adequate results can be

obtained by use of a PEG-600 standard that is not related to the pharmaceutical manufacturing waste stream under analysis and careful definition of an "elution range"[6] for PEG-600 in both external standards and samples.

18.3.1.6 Modified ASTM Method D3695-88

ASTM Method D3695-88 entitled "Standard Test Method for Volatile Alcohols in Water by Direct Aqueous-Injection Gas Chromatography" (9), modified as described below, is proposed as an alternative to Method 1671 for compliance monitoring for methanol, ethanol, and n-propanol in the pharmaceutical manufacturing industry. This modified Method is proposed because it may offer lower quantitation limits than proposed Method 1671 for these alcohols under some circumstances. Because ASTM methods in general, and ASTM Method D3695-88 in particular, do not incorporate the quality assurance/quality control standards found in methods used for filing applications and compliance monitoring under the NPDES, ASTM Method D3695-88 is modified by incorporation of certain of these quality control/quality assurance procedures and their respective numerical standards and limits described in Method 1671. The following procedures and corresponding Section in Method 1671 are incorporated into ASTM Method D3695-88 for purposes of analyses pursuant to NPDES permits:

- Operation of a formal quality assurance program (Section 9.1);
- Analysis of a matrix spike (MS) and a matrix spike duplicate (MSD) and adherence to the relative percent difference (RPD) standard listed and the recovery limits found in Table 3 (Section 9.3);
- Analysis of blanks (Section 9.4);
- Initial precision and accuracy, limited to methanol, ethanol, and n-propanol using the acceptance criteria found in Table 3 (Section 9.5);

[6]An "elution range" is defined as a characteristic period of time during which the derivatized PEG-600 elutes from the chromatographic column. This range should encompass at least 90 percent of the PEG-600 derivative in both the standard and sample.

- Analysis of field replicates (Section 9.7);
- Record keeping (Section 9.8); and
- Ongoing accuracy using the acceptance criteria found in Table 3 (Section 13.1).

18.4 Tables

Tables 18-1 through 18-7 provide additional information for each of the analytes proposed for the pharmaceutical manufacturing industry. Table 18-1 provides the list of analytes proposed for regulation with their chemical abstracts service registry numbers. Tables 18-2, 18-3, and 18-4 provide the analytical methods used for determination of conventional pollutants (and COD), priority pollutants, and nonconventional pollutants, respectively, in the studies leading up to the proposed rule supported by this document. Table 18-5 provides a list of the pharmaceutical manufacturing industry analytes with promulgated analytical methods while Table 18-6 provides a list of nonconventional pharmaceutical manufacturing industry analytes and the methods proposed for their determination. Table 18-7 provides a list of the pharmaceutical manufacturing industry analytes along with their respective minimum levels (MLs). In some cases, more than one ML is provided for an analyte in this table when more than one proposed method may be used for its determination.

Table 18-1

Pollutants Proposed for Regulation

Proposed Pollutant	CASRN
Conventional Pollutants	
Biological Oxygen Demand (BOD_5)	C-002 (a)
pH	C-006 (a)
Total suspended nonfilterable solids (TSS)	C-009 (a)
Priority Pollutants	
Benzene	71-43-2
Chlorobenzene	108-90-7
Chloroform	67-66-3
Chloromethane	74-87-3
Cyanide, Total	57-12-5
o-Dichlorobenzene	95-50-1
1,2-Dichloroethane	107-06-2
Methylene chloride	75-09-2
Phenol	108-95-2
Toluene	108-88-3
Nonconventional Pollutants	
Acetone	67-64-1
Acetonitrile	75-05-8
Ammonia (Ammonium hydroxide)	1336-21-6
Amyl acetate	628-63-7
Amyl alcohol	71-41-0
Aniline	62-53-3
2-Butanone	78-93-3
n-Butyl acetate	123-86-4

Table 18-1

(Continued)

Proposed Pollutant	CASRN
n-Butyl alcohol	71-36-3
tert-Butyl alcohol	75-65-0
Chemical Oxygen Demand (COD)	C-004 (a)
Cyclohexane	110-82-7
Diethylamine	109-89-7
Diethylether	60-29-7
N,N-Dimethylacetamide	127-19-5
Dimethylamine	124-40-3
N,N-Dimethylaniline	121-69-7
N,N-Dimethylformamide	68-12-2
Dimethylsulfoxide	67-68-5
1,4-Dioxane	123-91-1
Ethanol	64-17-5
Ethyl acetate	141-78-6
Ethylene glycol	107-21-1
Formaldehyde	50-00-0
Formamide	75-12-7
Furfural	98-01-1
n-Heptane (b)	142-82-5
n-Hexane (b)	110-54-3
Isobutyraldehyde	78-84-2
Isopropanol	67-63-0
Isopropyl acetate	108-21-4
Isopropylether	108-20-3

Table 18-1

(Continued)

Proposed Pollutant	CASRN
Methanol	67-56-1
Methylamine	74-89-5
Methyl cellosolve (2-methoxyethanol)	109-86-4
Methyl formate	107-31-3
Methylisobutyl ketone	108-10-1
2-Methylpyridine (α-picoline)	109-06-8
Petroleum naphtha (b)	8030-30-6
Poly(ethylene glycol)-600	25322-68-3
n-Propanol	71-23-8
Pyridine	110-86-1
Tetrahydrofuran	109-99-9
Trichlorofluoromethane	75-69-4
Triethylamine	121-44-8
m-Xylene	108-38-3
o-Xylene	95-47-6
p-Xylene	106-42-3

(a) These are synthetic CASRNs designed for use with the Environmental Monitoring Methods Index (EMMI).
(b) Petroleum naphtha concentration will be estimated as the sum of the concentrations of n-pentane, n-hexane, and n-heptane.

Table 18-2

Analytical Methods Used for Determination of Conventional Pollutants and COD

Pollutant (Synthetic CASRN)	Method
BOD_5 (C-002)	405.1
COD (C-004)	410.1, 410.2, 410.3 (a), 410.4
pH (b)(C-006)	150.1
TSS (C-009)	160.2

(a) May be used in saline waters.
(b) The Agency is not reproposing pH limitations under BPT, but the previously promulgated method is listed here for convenience.

Table 18-3

Analytical Methods Used for Determination of Priority Pollutants

Priority Pollutant (CASRN)	Method
Benzene (71-43-2)	1624
Chlorobenzene (108-90-7)	1624
Chloroform (67-66-3)	1624
Chloromethane (74-87-3)	1624
Cyanide, Total (57-12-5)	335.2, 335.3
o-Dichlorobenzene (95-50-1)	1625
1,2-Dichloroethane (107-06-2)	1624
Methylene chloride (75-09-2)	1624
Phenol (108-95-2)	1625
Toluene (108-88-3)	1624

Table 18-4

Analytical Methods Used for Determination of Nonconventional Pollutants

Nonconventional Pollutant (CASRN)	Method	Notes
Acetone (67-64-1)	1624	
Acetonitrile (75-05-8)	1624	Reverse search
Ammonium hydroxide (1336-21-6)	350.2	
n-Amyl acetate (628-63-7)	No EPA Analysis	
n-Amyl alcohol (71-41-0)	No EPA Analysis	
Aniline (62-53-3)	1625	
2-Butanone (78-93-3)	1624	
n-Butyl acetate (123-86-4)	No EPA Analysis	
n-Butyl alcohol (71-36-3)	1624 8015 8015	Hot purge Hot purge Direct injection (a)
tert-Butyl alcohol (75-65-0)	1624 8015 8015	Hot purge Hot purge Direct injection (a)
Cyclohexane (110-82-7)	No EPA Analysis	
Diethylamine (109-89-7)	No EPA Analysis	
Diethylether (60-29-7)	1624	
N,N,-Dimethylacetamide (127-19-5)	No EPA Analysis	
Dimethylamine (124-40-3)	No EPA Analysis	
N,N-Dimethylaniline (121-69-7)	No EPA Analysis	
N,N-Dimethylformamide (68-12-2)	1625	Reverse search
Dimethylsulfoxide (67-68-5)	No EPA Analysis	
1,4-Dioxane (123-91-1)	1624	
Ethanol (64-17-5)	1624 8015 8015	Hot purge Hot purge Direct injection (a)

Table 18-4

(Continued)

Nonconventional Pollutant (CASRN)	Method	Notes
Ethyl acetate (141-78-6)	8015	Direct injection (a)
Ethylene glycol (107-21-1)	No EPA Analysis	
Formaldehyde (50-00-0)	HPLC	Region IX method (precursor to method 8315)
Formamide (75-12-7)	No EPA Analysis	
Furfural (98-01-1)	No EPA Analysis	
n-Heptane (142-82-5)	1624	Reverse search
n-Hexane (110-54-3)	1624	Reverse search
Isobutyraldehyde (78-84-2)	No EPA Analysis	
Isopropanol (67-63-0)	1624 8015 8015	Hot purge Hot purge Direct injection (a)
Isopropyl acetate (108-21-4)	8015	Direct injection (a)
Isopropylether (108-20-3)	1624 8015 8015	Hot purge Hot purge Direct injection (a)
Methanol (67-56-1)	1624 8015 8015	Hot purge Hot purge Direct injection (a)
Methylamine (74-89-5)	No EPA Analysis	
Methyl cellosolve (109-86-4)	No EPA Analysis	
Methyl formate (107-31-3)	8015	Direct injection (a)
Methylisobutyl ketone (108-10-1)	1624	Reverse search
2-Methylpyridine (109-06-8)	1625	
Petroleum naphtha (8030-30-6)	1624	Reverse search
Polyethylene glycol 600 (25322-68-3)	No EPA Analysis	

Table 18-4

(Continued)

Nonconventional Pollutant (CASRN)	Method	Notes
n-Propanol (71-23-8)	1624 8015 8015	Hot purge Hot purge Direct injection (a)
Pyridine (110-86-1)	1625	Reverse search
Tetrahydrofuran (109-99-9)	1624	Reverse search
Trichlorofluoromethane (75-69-4)	1624	Reverse search
Triethylamine (121-44-8)	1624	Reverse search
m-Xylene (108-38-3)	1624	Reverse search
o-Xylene (95-47-6)	1624	Reverse search
p-Xylene (106-42-3)	1624	Reverse search

(a) Two sample introduction techniques are listed in the method: 5020 is direct injection of a headspace sample and 5030 is purge and trap. The former method was used here.

Table 18-5

Pollutants From the Pharmaceutical Manufacturing Industry With Promulgated Analytical Methods

Pollutant (CASRN)	Promulgated Analytical Method	Reference
Acetone (67-64-1)	1624B	40 CFR 136, Appendix A
Ammonia (Ammonium hydroxide) (1336-21-6)	350.1, 350.2, 350.3 (Ammonia as N)	40 CFR Part 136
Benzene (71-43-2)	1624B	40 CFR 136, Appendix A
BOD_5 (C-002) (a)	405.1	40 CFR Part 136
2-Butanone (78-93-3)	1624B	40 CFR 136, Appendix A
Chlorobenzene (108-90-7)	1624B	40 CFR 136, Appendix A
Chloroform (67-66-3)	1624B	40 CFR 136, Appendix A
Chloromethane (74-87-3)	1624B	40 CFR 136, Appendix A
COD (C-004) (a)	410.1, 410.2, 410.3, 410.4	40 CFR Part 136
Cyanide, Total (57-12-5)	335.2, 335.3	40 CFR Part 136
o-Dichlorobenzene (95-50-1)	1625B	40 CFR 136, Appendix A
1,2-Dichloroethane (107-06-2)	1624B	40 CFR 136, Appendix A
Diethylether (60-29-7)	1624B	40 CFR 136, Appendix A
1,4-Dioxane (123-91-1)	1624B	40 CFR 136, Appendix A
Methylene chloride (75-09-2)	1624B	40 CFR 136, Appendix A
pH (b) (C-006) (a)	150.1	40 CFR Part 136
Phenol (108-95-2)	1625B	40 CFR 136, Appendix A
α-Picoline (2-Methylpyridine)(109-06-8)	1625B	40 CFR 136, Appendix A
Toluene (108-88-3)	1624B	40 CFR 136, Appendix A
TSS (C-009) (a)	160.2	40 CFR Part 136

(a) These are synthetic CASRNs designed for use with the Environmental Monitoring Methods Index (EMMI).
(b) The Agency is not reproposing pH limitations under BPT, but the previously promulgated method is listed here for convenience.

Table 18-6

Nonconventional Pharmaceutical Manufacturing Industry Pollutants and Proposed Analytical Methods

Nonconventional Pollutant (CASRN)	Proposed Analytical Method
Acetonitrile (75-05-8)	1666 1671
n-Amyl acetate (628-63-7)	1666
n-Amyl alcohol (71-41-0)	1666
Aniline (62-53-3)	1665
n-Butyl acetate (123-86-4)	1666
n-Butyl alcohol (71-36-3)	1666
tert-Butyl alcohol (75-65-0)	1666
Cyclohexane (110-82-7)	1666
Diethylamine (109-89-7)	1666 1671
N,N-Dimethylacetamide (127-19-5)	1665
Dimethylamine (124-40-3)	1666 1671
N,N-Dimethylaniline (121-69-7)	1665
N,N-Dimethylformamide (68-12-2)	1665
Dimethylsulfoxide (67-68-5)	1666 1671
Ethanol (64-17-5)	1666 1671 Modified ASTM D3695-88
Ethyl acetate (141-78-6)	1666
Ethylene glycol (107-21-1)	1666 1671
Formaldehyde (50-00-0)	1667

Table 18-6

(Continued)

Nonconventional Pollutant (CASRN)	Proposed Analytical Method
Formamide (75-12-7)	1666 1671
Furfural (98-01-1)	1666 1667
n-Heptane (a) (142-82-5)	1666
n-Hexane (a) (110-54-3)	1666
Isobutyraldehyde (78-84-2)	1666 1667
Isopropanol (67-63-0)	1666
Isopropyl acetate (108-21-4)	1666
Isopropylether (108-20-3)	1666
Methanol (67-56-1)	1666 1671 Modified ASTM - D3695-88
Methylamine (74-89-5)	1666 1671
Methyl cellosolve (2-methoxyethanol)(109-86-4)	1666 1671
Methyl formate (107-31-3)	1666
Methylisobutyl ketone (108-10-1)	1666
2-Methylpyridine (α-picoline)(109-06-8)	1665
Petroleum naphtha (a) (8030-30-6)	1666
Polyethylene glycol 600 (25322-68-3)	1673
n-Propanol (71-23-8)	1666 1671 Modified ASTM - D3695-88

Table 18-6

(Continued)

Nonconventional Pollutant (CASRN)	Proposed Analytical Method
Pyridine (110-86-1)	1665
Tetrahydrofuran (109-99-9)	1666
Trichlorofluoromethane (75-69-4)	1666
Triethylamine (121-44-8)	1666 1671
m,p-Xylene (108-38-3 and 106-42-3)(b)	1666
o-Xylene (95-47-6)	1666

(a) Petroleum naphtha concentration will be estimated as the sum of the concentrations of n-pentane, n-hexane, and n-heptane.
(b) m-Xylene and p-xylene elute together and are indistinguishable in the analytical system.

Table 18-7

Proposed and Promulgated MLs for Pharmaceutical Manufacturing Industry Pollutants

Proposed Pollutant	Proposed or Promulgated Analytical Method	ML[a] units/Liter[c]
Conventional Pollutants		
Biological Oxygen Demand (BOD_5)	405.1	2 mg[d]
pH	150.1	NA
Total suspended nonfilterable solids (TSS)	160.2	4 mg[e]
Priority Pollutants		
Benzene	1624B	10 μg
Chlorobenzene	1624B	10 μg
Chloroform	1624B	10 μg
Chloromethane	1624B	50 μg
Cyanide, Total	335.2 335.3	20 μg[f] 5 μg[g]
o-Dichlorobenzene	1625B	10 μg
1,2-Dichloroethane	1624B	10 μg
Methylene chloride	1624B	10 μg
Phenol	1625B	10 μg
Toluene	1624B	10 μg
Nonconventional Pollutants		
Acetone	1624B	50 μg
Acetonitrile	1666 1671	5 mg 50 mg
Ammonia (Ammonium hydroxide)	350.1 350.2 350.3	10 μg[g] 50 μg[g] 30 μg[g]
Amyl acetate	1666	5 μg
Amyl alcohol	1666	500 μg

Table 18-7

(Continued)

Proposed Pollutant	Proposed or Promulgated Analytical Method	ML[a] units/Liter[c]
Aniline	1665	2 μg
2-Butanone	1624B	50 μg
n-Butyl acetate	1666	5 μg
n-Butyl alcohol	1666	500 μg
tert-Butyl alcohol	1666	100 μg
Chemical Oxygen Demand (COD)	410.1 410.2 410.3 410.4	NA NA NA NA
Cyclohexane	1666	5 μg
Diethylamine	1666 1671	200 mg 50 mg
Diethylether	1624B	50 μg
N,N-Dimethylacetamide	1665	50 μg
Dimethylamine	1666 1671	200 mg 50 mg
N,N-Dimethylaniline	1665	10 μg
N,N-Dimethylformamide	1665	5 μg
Dimethylsulfoxide	1666 1671	100 mg 20 mg
1,4-Dioxane	1624B	50 μg
Ethanol	1666 1671 Modified ASTM D3695-88	20 mg 50 mg 1 mg[h]
Ethyl acetate	1666	10 μg

Table 18-7

(Continued)

Proposed Pollutant	Proposed or Promulgated Analytical Method	ML[a] units/Liter[c]
Ethylene glycol	1666 1671	200 mg 100 mg
Formaldehyde	1667	50 μg
Formamide	1666 1671	1000 mg 100 mg
Furfural	1666 1667	500 μg 50 μg
n-Heptane (b)	1666	10 μg
n-Hexane (b)	1666	10 μg
Isobutyraldehyde	1666 1667	10 μg 50 μg
Isopropanol	1666	200 μg
Isopropyl acetate	1666	10 μg
Isopropylether	1666	5 μg
Methanol	1666 1671 Modified ASTM D3695-88	50 mg 50 mg 1 mg[h]
Methylamine	1666 1671	200 mg 50 mg
Methyl cellosolve (2-methoxyethanol)	1666 1671	50 mg 20 mg
Methyl formate	1666	100 μg
Methylisobutyl ketone	1666	10 μg
2-Methylpyridine (α-picoline)	1625B 1665	50 μg 5 μg
n-Pentane (b)	1666	10 μg

Table 18-7

(Continued)

Proposed Pollutant	Proposed or Promulgated Analytical Method	ML[a] units/Liter[c]
Petroleum naphtha (b)	1666	30 μg
Poly(ethylene glycol)-600	1673	1 mg
n-Propanol	1666 1671 Modified ASTM D3695-88	20 mg 50 mg 1 mg[h]
Pyridine	1665	5 μg
Tetrahydrofuran	1666	20 μg
Trichlorofluoromethane	1666	10 μg
Triethylamine	1666 1671	200 mg 50 mg
m,p-Xylene	1666	10 μg
o-Xylene	1666	5 μg

(a) The minimum level at which the entire analytical system shall give a recognizable signal and acceptable calibration points, taking into account method-specific sample and injection volumes. The ML is often calculated as 3.18 times the method detection limit (MDL). The ML was promulgated in 1984 at 40 CFR Part 136, Appendix A.
(b) Petroleum naphtha concentration will be estimated as the sum of the concentrations of n-pentane, n-hexane, and n-heptane.
(c) Units are either milligrams (mg) per liter or micrograms (μg) per liter. NA indicates that an ML is not applicable or that no ML is given in the method listed.
(d) "[E]stablished by the requirement for a minimum DO [dissolved oxygen] depletion of 2 mg/L."
(e) This is the lower end of the "practical range of the determination."
(f) The method is stated to be "sensitive to about 0.02 mg/L."
(g) This is the lower end of the "applicable range."
(h) The method states that the analytes can be "detected quantitatively in water and waste water at a minimum detection limit of 1 mg/L."

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5. Tou, J.C. Journal of Physical Chemistry, 78(11):1096-1098, 1974.

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9. "Standard Test Method for Volatile Alcohols in Water by Direct Aqueous-Injection Gas Chromatography." 1994 Annual Book of ASTM Standards, Volume 11.02 (Water (II)). ASTM, 1916 Race Street, Philadelphia, PA 19103-1187.

SECTION 19

GLOSSARY

Pharmaceutical Screener Questionnaire - A short questionnaire distributed by EPA to all known pharmaceutical facilities in June of 1989 in order to identify plants which manufacture pharmaceutical products.

Detailed Questionnaire - The 1990 Pharmaceutical Manufacturing Survey. A questionnaire sent by EPA to certain facilities in the pharmaceutical manufacturing industry in September 1991 to gather technical and financial information. The questionnaire was sent to those facilities likely to be affected by promulgation of revised effluent limitations guidelines, pretreatment standards, and new source performance standards for this industry.

Administrator - The Administrator of the U.S. Environmental Protection Agency.

Agency - The U.S. Environmental Protection Agency.

Annual average - The mean concentration, mass loading, or production-normalized mass loading of a pollutant over a period of 365 consecutive days (or such other period of time determined by the permitting authority to be sufficiently long to encompass expected variability of the concentration, mass loading, or production-normalized mass loading at the relevant point of measurement).

Average monthly discharge limitation - The highest allowable average of "daily discharges" over a calendar month, calculated as the sum of all "daily discharges" measured during the calendar month divided by the number of "daily discharges" measured during the month.

Backwashing - The operation of cleaning a multimedia filter by reversing the flow of water or liquid that is being filtered.

Batch operation - A pharmaceutical manufacturing operation consisting of a series of operating units which process predetermined specific amounts of materials and carry the process to completion before starting another cycle.

Bench-scale operation - Laboratory testing of materials, methods, or processes on a small scale, such as on a laboratory worktable.

BAT - The best available technology economically achievable, as described in Section 304(b)(2) of the Clean Water Act.

BCT - The best conventional pollutant control technology, as described in Section 304(b)(4) of the Clean Water Act.

BMP or BMPs - Best management practice(s), as described in Section 304(e) of the Clean Water Act.

Biological and natural extraction - The chemical and physical extraction of pharmaceutically active ingredients from natural sources such as plant roots and leaves, animal glands, and parasitic fungi. The process operations involving biological and natural extraction define Subcategory B (40 CFR 439, Subpart B).

BOD_5 - Five-day biochemical oxygen demand. A measure of biochemical decomposition of organic matter in a water sample. It is determined by measuring the dissolved oxygen consumed by microorganisms to oxidize the organic contaminants in a water sample under standard laboratory conditions of five days and 20°C. BOD_5 is not related to the oxygen requirements in chemical combustion.

Boiler - Any enclosed combustion device that extracts useful energy in the form of steam and is not an incinerator.

BPT - The best practicable control technology currently available, as described in Section 304(b)(1) of the Clean Water Act.

CAA - Clean Air Act. The Air Pollution Prevention and Control Act (42 U.S.C. 7401 et. seq.), as amended, inter alia, by the Clean Air Act Amendments of 1990 (Public Law 101-549, 104 Stat. 2399).

Chemical synthesis - The process(es) of using a chemical reaction or a series of chemical reactions to manufacture pharmaceutically active ingredients. The chemical synthesis process operations define Subcategory C (40 CFR 439, Subpart C).

CFR - Code of Federal Regulations, published by the U.S. Government Printing Office. A codification of the general and permanent rules published in the Federal Register by the Executive departments and agencies of the federal government. The Code is divided into 50 titles which represent broad areas subject to federal regulation. Each title is divided into chapters which usually bear the name of the issuing agency, and each chapter is divided into parts covering specific regulatory areas. Citations of the Code of Federal Regulations include title, part, and section number (e.g., 40 CFR 1.1 - title 40, part 1, and section 1).

Clarifier - A treatment unit designed to remove suspended materials from wastewater typically by sedimentation.

Closed vent system - A system that is not open to the atmosphere and is composed of piping, ductwork, connections, and, if necessary, flow-inducing devices that transport gas or vapor from an emission point to a control device or back into the process.

CN - Abbreviation for total cyanide.

COD - Chemical oxygen demand (COD) - A nonconventional bulk parameter that measures the total oxygen-consuming capacity of wastewater. This parameter is a measure of materials in water or wastewater that are biodegradable and materials that are resistant (refractory) to biodegradation. Refractory compounds slowly exert demand on downstream receiving water resources. Certain of the compounds measured by this parameter have been found to have carcinogenic, mutagenic, and similar adverse effects, either singly or in combination. It is expressed as the amount of oxygen consumed by a chemical oxidant in a specific test.

Combustion device - An individual unit of equipment, including but not limited to, an incinerator or boiler, used for the thermal oxidation of organic hazardous air pollutant vapors.

Condensate - Any material that has condensed from a gaseous phase into a liquid phase.

Continuous discharge - Discharge that occurs without interruption throughout the operating hours of the facility.

Continuous operation - A pharmaceutical manufacturing operation which may consist of a series of operating units which continuously process materials.

Controlled-release discharge - A discharge that occurs at a rate that is intentionally varied to accommodate fluctuations in receiving stream assimilative capacity or for other reasons.

Conventional pollutants - The pollutants identified in Section 304(a)(4) of the Clean Water Act and the regulations thereunder (i.e., biochemical oxygen demand (BOD_5), total suspended solids (TSS), oil and grease, fecal coliform and pH).

CWA - Clean Water Act. The Federal Water Pollution Control Act Amendments of 1972 (33 U.S.C. 1251 et seq.), as amended, inter alia, by the Clean Water Act of 1977 (Public Law 95-217) and the Water Quality Act of 1987 (Public Law 100-4).

Daily discharge - The discharge of a pollutant measured during any calendar day or any 24-hour period that reasonably represents a calendar day for purposes of sampling. For pollutants with limitations expressed in units of mass, the daily discharge is calculated as the total mass of the pollutant discharged over the day. For pollutants with limitations

expressed in other units of measurement, the daily discharge is calculated as the average measurement of the pollutant over the day.

Direct discharger - A facility that discharges or may discharge treated or untreated process wastewaters, non-contact cooling waters, or nonprocess wastewaters (including stormwater runoff) into waters of the United States.

Effluent - Wastewater discharges.

Effluent limitation - Any restriction, including schedules of compliance, established by a State or the Administrator on quantities, rates, and concentrations of chemical, physical, biological, and other constituents which are discharged from point sources into waters of the United States, the waters of the contiguous zone, or the ocean.

Emission - Passage of air pollutants into the atmosphere via a gas stream or other means.

Emission point - Any location within a source from which air pollutants are emitted, including an individual process vent, an opening within a wastewater collection and treatment system, or an open piece of process equipment.

EOP (end-of-pipe) effluent - Final plant effluent discharged to waters of the United States or to a POTW.

EOP (End-of-pipe) treatment - End-of-pipe treatment facilities or systems used to treat process wastewaters, nonprocess wastewaters (including stormwater runoff) after the wastewaters have left the process area of the facility and prior to discharge. End-of-pipe treatment generally does not include facilities or systems where products or by-products are separated from process wastewaters and returned to the process or directed to air emission control devices.

EPA - The U.S. Environmental Protection Agency.

Fermentation - A chemical change induced by a living organism or enzyme, specifically bacteria or the microorganisms occurring in unicellular plants such as yeast, molds, or fungi. Process operations that utilize fermentation to manufacture pharmaceutically active ingredients define Subcategory A (40 CFR 439, Subpart A).

FR - Federal Register, published by the U.S. Government Printing Office, Washington, D.C. A publication making available to the public regulations and legal notices issued by federal agencies. These include Presidential proclamations and Executive Orders and federal agency documents having general applicability and legal effect, documents required to be published by act of Congress and other federal agency documents of

public interest. Citations of the Federal Register include volume number and page number (e.g., 55 FR 12345).

General Provisions - General Provisions for national emission standards for hazardous air pollutants and other regulatory requirements pursuant to Section 112 of the CAA as amended November 15, 1990. The General Provisions, to be located in Subpart A of Part 63 of Title 40 of the Code of Federal Regulations, codify procedures and criteria to implement emission standards for stationary sources that emit (or have the potential to emit) one or more of the 189 chemicals listed as hazardous air pollutants in Section 112(b) of the CAA as amended in 1990. EPA published the NESHAP General Provisions in the Federal Register on March 16, 1993 (59 FR 12408). The term General Provisions also refers to the General Provisions for the effluent limitations guidelines and standards to be located at 40 CFR 439.

HAP - Hazardous Air Pollutant. Any of the 189 chemicals listed under Section 112(b) of the CAA.

Incinerator - An enclosed combustion device that is used for destroying organic compounds. Auxiliary fuel may be used to heat waste gas to combustion temperatures. Any energy recovery section present is not physically formed into one manufactured or assembled unit with the combustion section; rather, the energy recovery section is a separate section following the combustion section and the two are joined by ducts or connections carrying flue gas.

Indirect discharger - A facility that discharges or may discharge wastewaters into a publicly owned treatment works (POTW).

Individual drain system - The system used to convey process wastewater streams from the pharmaceutical manufacturing process equipment or tank, or process wastewater collection and treatment system unit. The term includes all process drains and junction boxes, together with their associated sewer lines and other junction boxes, manholes, sumps, and lift stations. The individual drain system shall be designed to segregate the vapors within the system from other drain systems. A separate storm sewer system, which is a drain and collection system designed and operated for the purpose of collecting storm runoff at a facility, and which is segregated from all other individual drain systems, is excluded from this definition.

In-plant control technologies - Controls or measures applied within the manufacturing process to reduce or eliminate pollutant and hydraulic loadings as well as technologies applied directly to wastewater generated by manufacturing processes such as steam stripping and cyanide destruction.

In-plant monitoring point - A monitoring point placed prior to dilution by non-process wastewater, commingling with other process wastestreams not containing the regulated pollutants at treatable levels, and any conveyance, equalization, or other treatment units which are open to the atmosphere.

In-plant monitoring point for cyanide - A monitoring point for cyanide which occurs in plant, prior to dilution or mixing with any noncyanide-bearing wastewater.

IU - Industrial User. Synonym for "Indirect Discharger."

Junction box - A manhole access point to a wastewater sewer system or a lift station.

LTM - Long-term mean. For purposes of the effluent guidelines, average pollutant levels achieved over a period of time by a facility, subcategory, or technology option. These LTMs were used in developing the limitations and standards for the proposed regulation.

MACT - Maximum Achievable Control Technology. Technology basis for the national emission standards for hazardous air pollutants.

Major source - As defined in Section 112(a) of the CAA, a major source is any stationary source or group of stationary sources located within a contiguous area and under common control that emits or has the potential to emit, considering controls, in the aggregate 10 tons per year or more of any hazardous air pollutant or 25 tons per year or more of any combination of hazardous air pollutants.

Maximum daily discharge limitation - The highest allowable daily discharge of a pollutant measured during a calendar day or any 24-hour period that reasonably represents a calendar day for purposes of sampling.

Methyl cellosolve - A trademark name for ethylene glycol monomethyl ether (q.v.).

Mg - Megagram. One million (10^6) grams, or one metric ton.

Metric ton - One thousand (10^3) kilograms (abbreviated as kkg), or one megagram. A metric ton is equal to 2,204.5 pounds.

Minimum level - The level at which an analytical system gives recognizable signals and an acceptable calibration point.

Mixing, compounding, or formulating - Process through which pharmaceutically active ingredients are put in dosage forms. Processes involving mixing, compounding, or formulating define Subcategory D (40 CFR 439, Subpart D).

Modification - As defined in Section 112(a) of the CAA, a modification is any physical change in, or change in the method of operation of, a major source which increases the actual emissions of any hazardous air pollutant emitted by such source by more than a *de minimis* amount or which results in the emission of any hazardous air pollutant not previously emitted by more than a *de minimis* amount.

NESHAP - National Emission Standard for Hazardous Air Pollutants. Emission standard promulgated under Section 112(d) of the CAA for hazardous air pollutants listed in Section 112(b) of the CAA.

New Source - As defined in 40 CFR 122.2, 122.29, and 403.3 (k), a new source is any building, structure, facility, or installation from which there is or may be a discharge of pollutants, the construction of which commenced (1) for purposes of compliance with New Source Performance Standards, after the promulgation of such standards being proposed today under CWA section 306; or (2) for the purposes of compliance with Pretreatment Standards for New Sources, after the publication of proposed standards under CWA section 307(c), if such standards are thereafter promulgated in accordance with that section.

Noncontinuous or intermittent discharge - Discharge of wastewaters stored for periods of at least 24 hours and released on a batch basis.

Nonconventional pollutants - Pollutants that are neither conventional pollutants nor toxic pollutants listed at 40 CFR Section 401.

Nondetect value - A concentration-based measurement reported below the minimum level that can reliably be measured by the analytical method for the pollutant.

Nonwater quality environmental impact - An environmental impact of a control or treatment technology, other than to surface waters.

NPDES - The National Pollutant Discharge Elimination System authorized under Section 402 of the CWA. The CWA requires NPDES permits for discharge of pollutants from any point source into waters of the United States.

NRDC - Natural Resources Defense Council.

NSPS - New source performance standards. This term refers to standards for new sources under Section 306 of the CWA.

Outfall - The mouth of conduit drains and other conduits from which a plant's effluent discharges into receiving waters.

Pharmaceutically active ingredient - Any substance considered to be an active ingredient by Food and Drug Administration regulations (21 CFR 210.3(6)(7)).

Pilot-scale - The trial operation of processing equipment which is the intermediate stage between laboratory experimentation and full-scale operation in the development of a new process or product.

Point of generation - The location where the process wastewater stream exits the pharmaceutical process equipment.

Point source category - A category of sources of water pollutants that are included within the definition of "point source" in Section 502(14) of the CWA.

Pollutant (to water) - Chemical constituent, dredged spoil, solid waste, incinerator residue, filter backwash, sewage, garbage, sewage sludge, munitions, chemical wastes, biological materials, certain radioactive materials, heat, wrecked or discarded equipment, rock, sand, cellar dirt, and industrial, municipal, and agricultural waste discharged into water. See CWA Section 502(6); 40 CFR 122.2.

POTW or POTWs - Publicly owned treatment works, as defined at 40 CFR 403.3(o).

Pretreatment standard - A regulation specifying industrial wastewater effluent quality required for discharge to a POTW.

Priority pollutants - The toxic pollutants listed in 40 CFR Part 423, Appendix A.

Process changes - Alterations in process operating conditions, equipment, or chemical use that reduce the formation of chemical compounds that are pollutants and/or pollutant precursors.

Process emission point - A gas stream that contains hazardous air pollutants discharged during operation of process equipment. Process emission points include gas streams that are discharged directly to the atmosphere, discharged to the atmosphere via vents or open process equipment, or after diversion through a product recovery device.

Process unit - A piece of equipment, such as a chemical reactor or fermentation tank, associated with pharmaceutical manufacturing operations.

Process wastewater - Any water that, during manufacturing or processing, comes in direct contact with or results from the production or use of any raw material, intermediate product, finished product, by product, or waste product. Process wastewater includes surface runoff from the immediate process area that has the potential to become contaminated. Noncontact cooling waters, utility wastewaters, general site surface runoff,

groundwater, and other water generated on site that are not process wastewaters are specifically excluded from this definition.

Process wastewater collection system - A piece of equipment, structure, or transport mechanism used in conveying or storing a process wastewater stream. Examples of process wastewater collection system equipment include individual drain systems, wastewater tanks, surface impoundments, and containers.

Process wastewater stream - When used in connection with CAA obligations, any HAP-containing liquid that results from either direct or indirect contact of water with organic compounds.

Process water - Water used to dilute, wash, or carry raw materials, and any other materials used in pharmaceutical manufacturing processes.

Product - Completed material ready for sale or intra-company off-site transfer.

PSES - Pretreatment standards for existing sources of indirect discharges, under Section 307(b) of the CWA.

PSNS - Pretreatment standards for new sources of indirect discharges, under Section 307(b) and (c) of the CWA.

RCRA - Resource Conservation and Recovery Act of 1976, as amended (42 U.S.C. 6901, et seq.).

Research - Bench-scale activities or operations used in research and/or product development of a pharmaceutical product. The Research operations define Subcategory E (40 CFR 439, Subpart E).

SIC - Standard Industrial Classification. A numerical categorization system used by the U.S. Department of Commerce to denote segments of industry. An SIC code refers to the principal product, or group of products, produced or distributed, or to services rendered by an operating establishment. SIC codes are used to group establishments by the primary activity in which they are engaged.

Source category - A category of major or area sources of hazardous air pollutants.

Source reduction - The reduction or elimination of waste generation at the source, usually within a process. Any practice that: 1) reduces the amount of any hazardous substance, pollutant, or contaminant entering any waste stream or otherwise released into the environment (including fugitive emissions) prior to recycling, treatment, or disposal; and 2) reduces the hazards to public health and the environment associated with the release of such substances, pollutants, or contaminants.

Stationary source - Any building, structure, facility, or installation that emits or may emit any air pollutant. See CAA Section 111(a)(3).

TSS - Total suspended solids.

Toxic pollutants - the pollutants designated by EPA as toxic in 40 CFR Part 401.15. Also known as priority pollutants.

TWF - Toxic weighting factor.

VF - Variability factor. The daily variability factor is the ratio of the estimated 99th percentile of the distribution of daily values divided by the expected value, or mean, of the distribution of the daily data. The monthly variability factor is the estimated 95th percentile of the monthly averages of the data divided by the expected value of the monthly averages.

Waters of the United States - The same meaning set forth in 40 CFR 122.2.

Zero discharge - No discharge of wastewater to waters of the United States or to a POTW.

APPENDIX A
GUIDANCE FOR IMPLEMENTING THE PHARMACEUTICAL MANUFACTURING INDUSTRY REGULATIONS

1.0 INTRODUCTION

This appendix is intended to serve as an aid in implementing the Pharmaceutical Manufacturing Industry Point Source Category Effluent Limitations Guidelines, Pretreatment Standards and New Source Performance Standards. This appendix presents the development of permit limitations for several hypothetical plants that illustrate by example how the proposed pharmaceutical manufacturing industry effluent limitations guidelines and standards are to be implemented.

Five permit case studies are presented:

Case 1: BPT and BAT limitations for a multiple subcategory facility.

Case 2: PSES for a multiple subcategory facility.

Case 3: NSPS for a multiple subcategory facility.

Case 4: PSNS for a multiple subcategory facility.

Case 5: BPT and BAT limitations for a facility with pharmaceutical manufacturing and organic chemicals manufacturing operations.

The examples presented here have been selected to cover direct and indirect dischargers as well as new and existing sources. Special circumstances have been built into each example to illustrate how a permit writer would be advised to handle these cases. The plants presented here may not represent an average cross section of the industry, but they have been selected for their illustrative value.

As discussed in the body of the Technical Development Document (TDD), the Pharmaceutical Manufacturing Industry effluent limitations guidelines and standards are concentration based and adhere to the "building block" concept. Each regulated wastestream in an outfall is assigned a mass-based discharge allowance based on a calculation of its applicable concentration-based limitation and annual average flow. The sum of the allowances is the total mass discharge allowance for the outfall. The examples that follow assume some familiarity with the "building block" concept as well as familiarity with the material presented in the pharmaceutical manufacturing industry preamble, proposed regulations, and main body of the TDD.

Mass limitations for unregulated process wastewater streams and dilution streams at direct discharging facilities are established by the NPDES permit authority using best professional judgement (BPJ). Mass limitations for unregulated process wastewater streams and dilution streams at indirect discharging facilities are established by the Control Authority (see 40 CFR 403.12(a), and 40 CFR 403.3) by using the combined wastestream formula (see 40 CFR 403.6(e)(i), (ii)).

The following reference is recommended to complement this document:

- "Training Manual for NPDES Permit Writers," U.S. Environmental Protection Agency, Office of Water, Washington, D.C., EPA833-B-93-003, March 1993.

Permit limits are generally expressed in terms of allowable mass (in units of pounds or kilograms) of pollutant per day. However, the pharmaceutical industry regulations are concentration based. To convert the concentration-based limitations to mass-based limitations an accurate determination of the annual average process wastestream flows will have to be determined by the permit writer. The following discussion is designed to aid the permit writer in this process.

1.1 Calculation of Annual Average Process Wastewater Discharge

"Process wastewater discharge" is defined by 40 CFR 122.2 to include wastewaters resulting from manufacture of pharmaceutical products that come in direct contact with raw materials, intermediate products, and final products, and surface runoff from the immediate process area that has the potential to become contaminated. Noncontact cooling waters, utility wastewaters, general site surface runoff, groundwater, and other nonprocess water generated on site are specifically excluded from this definition. The appropriate process wastewater discharge flow for each stream to be used when developing mass-based limitations must be determined by the permitting or control authority on a case-by-case basis using current information provided by the applicant. In cases where the permit writer deems the process wastewater discharge flow claimed by industry to be excessive, he/she may develop a more appropriate process wastewater discharge flow for use in computing the mass-based permit limitations. The permit writer should review the following items to evaluate whether process wastewater discharge flow is excessive:

- The component flows to ensure that the claimed flows are, in fact, process wastewater discharge flows as defined by 40 CFR 122.2.

- The plant operations to ensure that sound water conservation practices are being followed. Examples include minimization of process water uses and reuse or recycle of intermediate process waters or treated wastewaters at the process area and in wastewater treatment operations (pump seals, equipment and area washdowns, etc.)

- Barometric condenser use at the process level. Often, barometric condensers will generate relatively large volumes of slightly contaminated water. Replacing barometric condensers with surface condensers can reduce wastewater volumes significantly and result in collection of condensates that may be returned to the process.

To establish a NPDES permit for a direct discharging facility, the permit writer should determine which subcategories the facility's operations fall within and use the corresponding concentration-based effluent limitations as a basis for developing the mass-based limitations. The permit writer should then determine the facility's annual average process wastewater discharge flow (i.e., the permit writer should consider only the sources of "process wastewater discharge," as defined previously, when determining the annual average process wastewater discharge flow; nonprocess wastewater discharges should not be included). The annual average flow is defined as the average of daily flow measurements calculated over at least a year (1); however, if available, multiple years' data are preferable to obtain a representation of average daily flow.

The permit writer is advised to establish, for each point source discharge, a single estimate of the regulated long-term average daily flow measurements based on three to five years of facility data. (1) In the event that no historical data or actual process wastewater flow data exist (such as for a new source), the permit writer is advised to establish a reasonable estimate of the facility's projected flow. This may include a request for the facility to measure process wastewater flows for a representative period of time to establish a flow basis. The permit writer is advised to establish a flow rate that is expected to be representative during the entire term of the permit. If a plant is planning significant changes in production during the effective period of the permit, the permitting authority may consider establishing multiple tiers of limitations as a function of these changes. Alternatively, a permit may be modified during its term, either at the request of the permittee, permitter, or another party, or on EPA's initiative, to increase or decrease the flow basis in response to a significant change in production (40 CFR 124.5, 122.62). A change in production may be an "alteration" of the permitted activity or "new information" that would provide the basis for a permit modification (40 CFR 122.62(a)).

1.2 Calculation of Mass-Based Permit Limitations

After determining the facility's annual average process wastewater flow, the permit writer should use the annual average process wastewater discharge flow to convert concentration-based limitations into mass-based limitations. The following equation can be used by the permit writer to convert a concentration-based limitation into a mass-based limitation:

$$L_m = L_c \times F \times k_1$$

where:

L_M	=	mass-based effluent limitation, lbs/day
L_C	=	concentration-based limitation, mg/L
F	=	average process wastewater discharge, gal/day
k_1	=	unit conversion factor, (L × lbs)/(gal × mg).

For this example, the unit conversion factor, k_1 is used to convert from [(mg/L)×(gal/day)] to (lbs/day) as follows:

$$k = \frac{1\,L}{0.264179\,gal} \times \frac{1\,g}{1{,}000\,mg} \times \frac{1\,lb}{453.592\,g} = 8.345 \times 10^{-6} \times \frac{L \times lb}{gal \times mg}$$

If the concentration based limitations are expressed as μg/L, the unit conversion factor k_2 can be used to convert from [(μg/L) × (gal/day)] to (lbs/day) as follows:

$$k_2 = \frac{1\ L}{0.264179\ gal} \times \frac{1\ g}{1{,}000{,}000\ \mu g} \times \frac{1\ lb}{453.592\ g} = 8.345 \times 10^{-9} \times \frac{L \times lb}{gal \times \mu g}$$

2.0 CASE STUDY 1, BPT AND BAT EFFLUENT LIMITATIONS FOR A MULTIPLE SUBCATEGORY FACILITY

Plant A is an existing multiple subcategory, direct discharging pharmaceutical manufacturing facility. A wastewater flow schematic for this facility is presented in Figure A-1.

2.1 BPT Effluent Limitations

The revised BPT effluent limitations guidelines establish new BOD_5, COD, and TSS effluent limitations for Subcategory A, B, C, and D operations at direct discharging facilities. The pH effluent limit, established in the 1976 final rule to be in the range of 6.0 to 9.0 standard units for all subcategories, will not be amended. The BPT effluent limitations for Subcategory E bench-scale operations, established in the 1983 final rule, will not be amended. As discussed in Section 6.2 of the TDD, the other conventional pollutants, such as fecal coliform and oil & grease, will not be regulated by BPT for the pharmaceutical manufacturing point source category.

The proposed effluent limitations guidelines are concentration-based and, as such, do not regulate wastewater flow. The permit writer must use a reasonable estimate of process wastewater discharge flow and the concentration-based limitations to develop mass-based limitations for the NPDES permit. Table 13-1 of the TDD presents the proposed maximum daily and monthly average BPT effluent limitations for Subcategory A, B, C, and D operations at direct discharging facilities.

The limitations for BOD_5, COD, and TSS will be applied to the final effluent. An example calculation of the BPT maximum for any one day and monthly average BOD_5 limitations for this facility is shown in 2.1.1 and 2.1.2.

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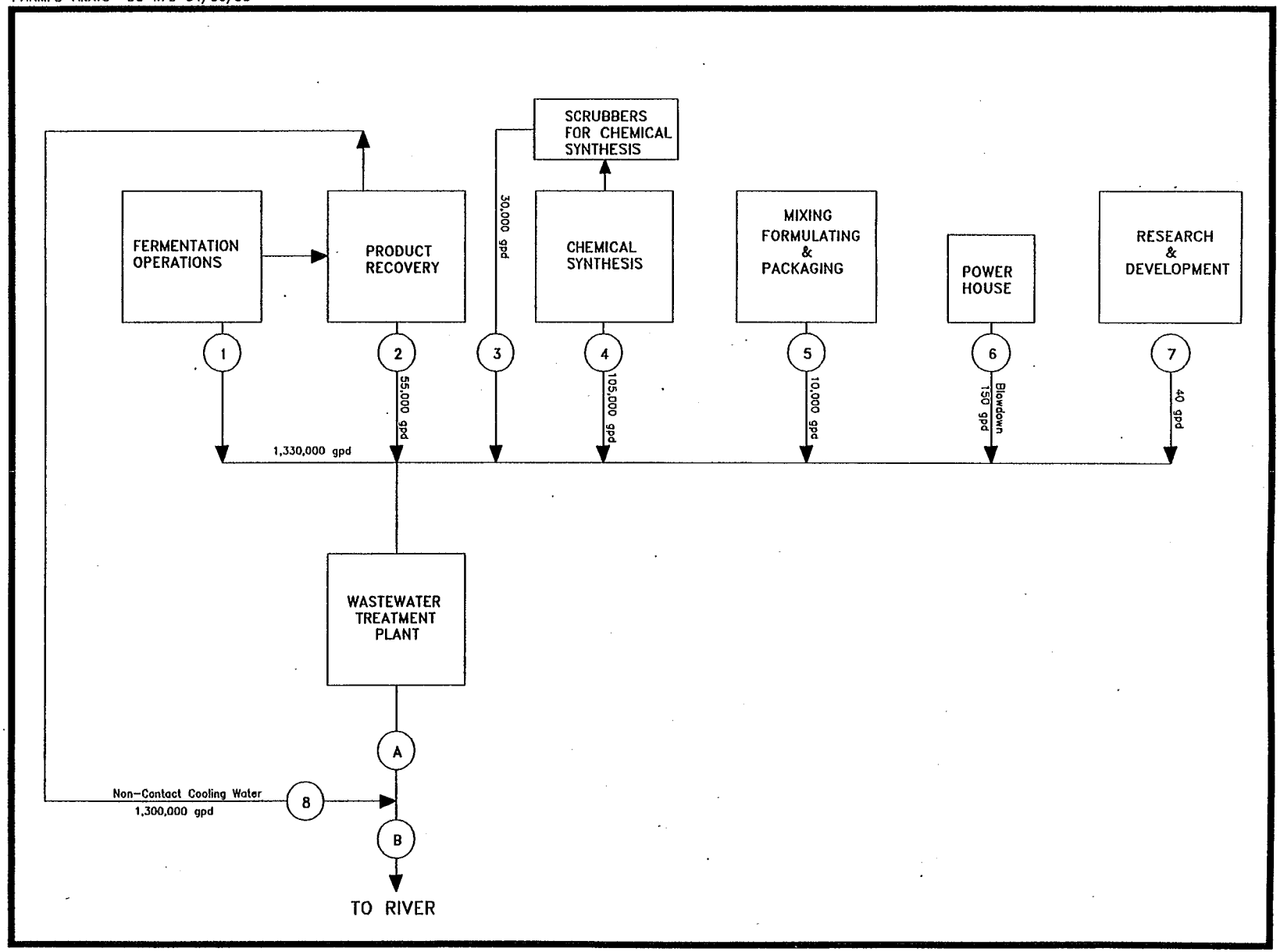

Figure A-1. Flow Schematic for Facility A.

2.1.1 Maximum Effluent Limitations for Any One Day

The first step in establishing permit limitations is to determine the types of wastestreams (i.e., regulated process, unregulated process, and dilute). The flow breakdown for Facility A would look like this:

Waste Stream	Flow (gal/day)	
1. Fermentation Operations	1,330,000	(Regulated, Sub. A)
2. Product Recovery	55,000	(Regulated, Sub. A)
3. In-plant Scrubbers for Chemical Synthesis	30,000	(Regulated, Sub. C)
4. Chemical Synthesis	105,000	(Regulated, Sub. C)
5. Mixing, Formulating, and Packaging	10,000	(Regulated, Sub. D)
6. Boiler Blowdown	150	(Dilute)
7. Research and Development	40	(Regulated, Sub. E)*
8. Noncontact Cooling Waters	1,300,000	(Dilute)
Total Wastewater Flow:	2,830,190	
Total Regulated Process:	1,530,040	
Total Unregulated Process:	0	
Total Dilute:	1,300,150	

*For monthly average limitations only

Under BPT, streams 1, 2, 3, 4, 5, and 7 are considered regulated wastestreams as effluent limitations have been established for fermentation operations (Subcategory A), chemical synthesis operations (Subcategory C), formulating operations (Subcategory D), and research operations (Subcategory E). Air pollution control wastewaters are considered process wastewaters corresponding to the subcategory operations the air pollution control devices control. We have assumed the permit writer has sufficient information to

determine that the noncontact cooling waters do not have treatable levels of BPT pollutants.

Table 13-1 of the TDD presents the proposed maximum daily and monthly average BPT effluent limitations for Subcategory A, B, C, and D operations at direct discharging facilities. Daily maximum limitations have not been promulgated for Subcategory E operations. Monthly average limitations for Subcategory E operations have been promulgated and are presented in 40 CFR §439.52. (2). Since maximum limitations for any one day have not been promulgated for Subcategory E operations, wastestream 7 has been considered an unregulated wastestream in the calculation of daily maximum limitations. The total BPT maximum allowable discharge for any one day can be calculated by determining the mass discharge allowance using the combined wastestream formula (CWF) shown below:

$$M_T = \left[\sum_{i=1}^{N} M_i\right] \times \left[\frac{F_T - F_D}{\sum_{i=1}^{N} F_i}\right]$$

where:

M_T	=	Alternative mass limit for the pollutant in the combined wastestream (mass per day).
M_i	=	Treatment standard for the pollutant in the regulated stream i (mass per day)
F_i	=	Average daily flow (at least 30 day average) of the regulated stream i
F_D	=	Average daily flow (at least 30 day average) of dilute wastestream(s) entering the combined treatment system
F_T	=	Average daily flow (at least 30 day average) through the combined treatment facility (including regulated, unregulated, and dilute wastestreams)
N	=	Total Number of regulated streams

In this example, the previously listed variables are calculated as follows:

M_1 = Mass limit of BOD_5 in stream 1
M_1 = 139.7 mg/L × 1,330,000 gal/day × 8.345 × 10^{-6} = 1,550.5 lbs/day
M_2 = Mass limit of BOD_5 in stream 2
M_2 = 139.7 mg/L × 55,000 gal/day × 8.345 × 10^{-6} = 64.1 lbs/day
M_3 = Mass limit of BOD_5 in stream 3
M_3 = 139.7 mg/L × 30,000 gal/day × 8.345 × 10^{-6} = 35.0 lbs/day
M_4 = Mass limit of BOD_5 in stream 4
M_4 = 139.7 mg/L × 105,000 gal/day × 8.345 × 10^{-6} = 122.4 lbs/day
M_5 = Mass limit of BOD_5 in stream 5
M_5 = 36.5 mg/L × 10,000 gal/day × 8.345 × 10^{-6} = 3.0 lbs/day
M_6 = M_7 = M_8 = 0 (since these streams are considered dilution or unregulated process wastewater)
F_T = Total flow = 2,830,190 gpd
F_D = Dilution flow = 1,330,150
F_1 = Flow in stream 1 = 1,330,000
F_2 = Flow in stream 2 = 55,000
F_3 = Flow in stream 3 = 30,000
F_4 = Flow in stream 4 = 105,000
F_5 = Flow in stream 5 = 10,000

$$M_T = \frac{1{,}775 \text{ lbs}}{\text{day}} \times \left[\frac{2{,}830{,}190 \text{ gpd} - 1{,}300{,}150 \text{ gpd}}{1{,}530{,}000 \text{ gpd}}\right] = 1{,}775 \text{ lbs/day}$$

Therefore, maximum day effluent limitations for BOD_5 in the combined wastestream would be 1,775 lbs/day.

COD and TSS maximum day effluent limitations can be calculated in a similar manner.

2.1.2 Monthly Average Effluent Limitations

As mentioned previously, monthly average limitations for Subcategory E operations are not being amended from the 1983 final rule. These limitations are presented in 40 CFR §439.52(2). According to the 1983 final rule, the monthly average mass of BOD_5 shall

reflect not less than 90 percent reduction of BOD_5 multiplied by a variability factor of 3.0. However, a facility shall not be required to attain a monthly average BOD_5 effluent limitation of less than 45 mg/L. Assuming this facility has a concentration of 200 mg/L of BOD_5 from Subcategory E operations, a 90 percent reduction would be required, making the monthly average limitation 20 mg/L. After multiplying by a variability factor of 3.0, the monthly average effluent limitation for BOD_5 from Subcategory E operations is 60 mg/L. This limit is added to the monthly average limitations from the other subcategories to determine the total monthly average effluent limitation for BOD_5.

The total monthly average BPT BOD_5 limitations can be calculated as follows:

Stream 1 (Sub. A): $(57.8 \text{ mg/L} \times 1{,}330{,}000 \text{ gal/day} \times 8.345 \times 10^{-6}) = 641.5 \text{ lbs/day}$
Stream 2 (Sub. A): $(57.8 \text{ mg/L} \times 55{,}000 \text{ gal/day} \times 8.345 \times 10^{-6}) = 26.5 \text{ lbs/day}$
Stream 3 (Sub. C): $(57.8 \text{ mg/L} \times 30{,}000 \text{ gal/day} \times 8.345 \times 10^{-6}) = 14.5 \text{ lbs/day}$
Stream 4 (Sub. C): $(57.8 \text{ mg/L} \times 105{,}000 \text{ gal/day} \times 8.345 \times 10^{-6}) = 50.6 \text{ lbs/day}$
Stream 5 (Sub. D): $(11.2 \text{ mg/L} \times 10{,}000 \text{ gal/day} \times 8.345 \times 10^{-6}) = 0.9 \text{ lbs/day}$
Stream 7 (Sub. E): $(60 \text{ mg/L} \times 40 \text{ gal/day} \times 8.345 \times 10^{-6}) = 0.02 \text{ lbs/day}$

Total = 734 lbs BOD_5/day

The monthly average effluent limitation for BOD_5 in the combined wastestream would be 734 lbs/day.

This monthly average limitation is compared to the average of all daily mass discharge amounts in a calendar month to determine facility compliance.

COD and TSS monthly average effluent limitations can be calculated in a similar manner.

2.2 BAT Effluent Limitations

Tables 15-2 and 15-3 of the TDD present the proposed maximum daily and monthly average BAT effluent limitations guidelines for Subcategories A and C, and Subcategories B and D, respectively. BAT for ammonia and the organic pollutants listed in these tables are applicable to the final effluent discharged to the waters of the United States.

BAT limitations for cyanide are presented in Table 15-2 of the TDD, and are applicable to those wastewaters from Subcategory A and C operations known or believed to contain cyanide. Compliance monitoring for cyanide should occur in-plant, prior to dilution or mixing with any non-cyanide bearing wastewater. In-plant monitoring is required to prevent compliance through dilution with non-cyanide bearing wastewaters.

We will assume that facility A has provided the permit writer with an accurate characterization of its process wastestreams by means available such as solvent use and disposition data, and analytical scans of each stream. Permit limitations should be established and compliance monitoring required for each regulated pollutant listed on Table 15-1 generated or used at a pharmaceutical manufacturing facility. Limitations and routine compliance monitoring are not required for regulated pollutants not generated or used at a facility. A determination that regulated pollutants are not generated or used should be based on a review of all raw materials used, and an assessment of all chemical processes used, considering resulting products and by-products. The determination that a regulated pollutant is not generated or used must be confirmed by annual chemical analyses of wastewater from each monitoring location. Such confirmation is provided by an analytical measurement of a non-detect value.

The following presents a summary of the regulated pollutants expected to be found in this facility's wastestreams:

Stream	Subcategory	Flow (gal/day)	Pollutant
1	A	1,330,000	Methylene chloride, cyclohexane, acetone
2	A	55,000	Methylene chloride, methanol, acetone
3	C	30,000	Methanol
4	C	105,000	Methylene chloride, acetone, methanol, aniline
5	D	10,000	Aniline, cyclohexane
6	N/A	150	No BAT pollutants
7	E	40	No organic pollutants

Based on the above data, permit limitations are established for methylene chloride, cyclohexane, acetone, methanol, and aniline. All of these pollutants are listed in Table 15-1 of the TDD.

While Subcategory E bench-scale research wastewater is unregulated for the organic pollutants listed in streams 1-5 according to the definition in the General Pretreatment Regulations, Control Authorities have the authority to determine whether unregulated streams should be considered dilution under 40 CFR §403.6(d). Since organic pollutants were not found to be present in Subcategory E wastewater in this example, this wastestream is considered here as dilution water and no mass allowances for this wastewater will be given.

2.2.1 BAT Maximum Limitations for Any One Day

As shown in Tables 15-2 and 15-3 of the TDD, cyclohexane has a maximum daily limitation of non-detect (ND) for A, B, C, and D subcategories. Methylene chloride, acetone, and methanol have maximum daily limitations of ND in Subcategories A and C and a maximum daily numerical limitation in Subcategory D. Aniline has a maximum daily numerical limitation in A, B, C, and D subcategories.

The Subcategory A, C, and D maximum daily limitations for cyclohexane are all ND. Non-detect values are concentration-based measurements reported below the minimum level that can be reliably measured by the analytical method for the pollutant. Therefore, the permit limitation for cyclohexane should specify ND for all measurements. Any concentration measurements greater than the ND value for the pollutant are considered out of compliance.

The limitations for methylene chloride, acetone, and methanol for Subcategories A and C are ND. However, these pollutants have a numerical limitation for Subcategory D. Since monitoring points for organic pollutants under BAT are at end-of-pipe locations and Subcategory A, C, and D wastewater will most likely be combined at this location, a mass limitation for the combined wastestream can be determined by using the numerical value of the minimum level for these pollutants to determine the Subcategory A and C portion of the mass limitation.

The total BAT maximum allowable discharge for methanol for any one day can be calculated by determining the mass discharge allowance for each individual process stream and summing, as shown below.

Stream 1 (Sub. A): $(3{,}180\ \mu g/L \times 1{,}330{,}000\ gal/day \times 8.345 \times 10^{-9}) = 35.3\ lbs/day$
Stream 2 (Sub. C): $(3{,}180\ \mu g/L \times 55{,}000\ gal/day \times 8.345 \times 10^{-9}) = 1.46\ lbs/day$
Stream 3 (Sub. C): $(3{,}180\ \mu g/L \times 30{,}000\ gal/day \times 8.345 \times 10^{-9}) = 0.80\ lbs/day$

Stream 4 (Sub. C): (3,180 μg/L $\times$ 105,000 gal/day $\times$ 8.345 $\times$ 10^{-9}) = 2.79 lbs/day
Stream 5 (Sub. D): (6,660 μg/L $\times$ 10,000 gal/day $\times$ 8.345 $\times$ 10^{-9}) = 0.56 lbs/day

Total = 40.9 lbs/day
Total Facility Maximum Day Discharge for Methanol = 40.9 lbs/day

Maximum day effluent limitations for acetone and methylene chloride can be calculated in a similar manner.

Aniline has a numerical limitation for all subcategories. The concentration-based limitations in Tables 15-2 and 15-3 of the TDD should be converted to maximum day mass-based limitations as shown below:

Stream 1 (Sub. A): (10 μg/L $\times$ 1,330,000 $\times$ 8.345 $\times$ 10^{-9}) = 0.11 lbs/day
Stream 2 (Sub. A): (10 μg/L $\times$ 55,000 $\times$ 8.345 $\times$ 10^{-9}) = 0.0046 lbs/day
Stream 3 (Sub. C): (10 μg/L $\times$ 30,000 $\times$ 8.345 $\times$ 10^{-9}) = 0.0025 lbs/day
Stream 4 (Sub. C): (10 μg/L $\times$ 105,000 $\times$ 8.345 $\times$ 10^{-9}) = 0.0088 lbs/day
Stream 5 (Sub. D): (10 μg/L $\times$ 10,000 $\times$ 8.345 $\times$ 10^{-9}) = 0.0008 lbs/day

Total = 0.13 lbs/day
Total Facility Maximum Day Discharge for Aniline = 0.13 lbs/day

It will be critical in this example to monitor the plant effluent at monitoring Point A; prior to dilution with non-contact cooling waters. The limitations for most pollutants are based on treating the pollutant to levels near or below the analytical minimum level. Achieving such levels in part through dilution is not considered treatment and is not acceptable.

2.2.2 BAT Monthly Average Limitations for Organic Pollutants

The monthly average limitations for cyclohexane are ND for all subcategories, just like the cyclohexane maximum daily limitations. Section 2.2.1 explains how these concentration-based limitations are implemented.

The published monthly average limitations for methanol are ND for all subcategories. However, since the maximum daily limitation for Subcategory D is not ND, measurements above the minimum level are permitted. Within the course of a month, the average value of all measurements should be equal to or less than the minimum level of 3,180 μg/L. The corresponding monthly average mass-based limitation for this concentration is shown below.

Stream 1 (Sub. A): (3,180 μg/L $\times$ 1,330,000 gal/day $\times$ 8.345 $\times$ 10^{-9}) = 35.3 lbs/day
Stream 2 (Sub. A): (3,180 μg/L $\times$ 55,000 gal/day $\times$ 8.345 $\times$ 10^{-9}) = 1.46 lbs/day
Stream 3 (Sub. C): (3,180 μg/L $\times$ 30,000 gal/day $\times$ 8.345 $\times$ 10^{-9}) = 0.80 lbs/day
Stream 4 (Sub. C): (3,180 μg/L $\times$ 105,000 gal/day $\times$ 8.345 $\times$ 10^{-9}) = 2.79 lbs/day
Stream 5 (Sub. D): (3,180 μg/L $\times$ 10,000 gal/day $\times$ 8.345 $\times$ 10^{-9}) = 0.27 lbs/day

Total = 39.8 lbs/day
Monthly average discharge limitation for Methanol = 39.8 lbs/day

The monthly average for methylene chloride and acetone for Subcategories A and C are ND. These pollutants have numerical limitations for Subcategory D. This same scenario is described in Section 2.2.1. Using the methodology explained in Section 2.2.1, the monthly average limitations for methylene chloride are shown below:

Stream 1 (Sub. A): (10 μg/L $\times$ 1,330,000 gal/day $\times$ 8.345 $\times$ 10^{-9}) = 0.11 lbs/day
Stream 2 (Sub. A): (10 μg/L $\times$ 55,000 gal/day $\times$ 8.345 $\times$ 10^{-9}) = 0.0046 lbs/day
Stream 3 (Sub. C): (10 μg/L $\times$ 30,000 gal/day $\times$ 8.345 $\times$ 10^{-9}) = 0.0025 lbs/day
Stream 4 (Sub. C): (10 μg/L $\times$ 105,000 gal/day $\times$ 8.345 $\times$ 10^{-9}) = 0.0088 lbs/day
Stream 5 (Sub. D): (357 μg/L $\times$ 10,000 gal/day $\times$ 8.345 $\times$ 10^{-9}) = 0.03 lbs/day

Total = 0.16 lbs/day
Monthly average discharge limitation for methylene chloride = 0.16 lbs/day

Monthly average limitations for acetone can be calculated in the same manner.

The monthly average limitations for aniline are the same as the daily maximum limitations for aniline in all subcategories. Calculation of corresponding mass-based limitations are shown in Section 2.2.1.

3.0 CASE STUDY 2, PSES FOR A MULTIPLE SUBCATEGORY FACILITY

Facility B is an existing multiple subcategory indirect discharging pharmaceutical plant. A wastewater flow schematic for this facility is presented in Figure A-2.

3.1 PSES Permit Limitations

Two scenarios will be presented for PSES, the first will apply under co-proposal 1 and the second will apply under co-proposal 2. Co-proposal 1 for Subcategories A and C sets in-plant standards for 13 pollutants and end-of-pipe standards for 33 pollutants. Co-proposal 2 for Subcategories A and C sets in-plant standards for 13 pollutants, but has no end-of-pipe standards except for ammonia. Cyanide and ammonia are not regulated in Subcategories B and D. Co-proposal 1 for Subcategories B and D sets in-plant standards for 12 pollutants and end-of-pipe standards for 32 pollutants. Co-proposal 2 for Subcategories B and D sets in-plant standards for 12 pollutants, but has no end-of-pipe standards.

3.2 PSES Permit Limitations for Co-Proposal 1

Table 17-4 of the TDD presents the proposed daily maximum and monthly average PSES for Subcategories A, B, C, and D. The proposed standards are concentration-based and, as such, do not regulate wastewater flow. Organics being controlled under PSES have been divided into two groups, one list for organics to be controlled in-plant, and a second list of less volatile organics that are controlled at the end-of-pipe.

PSES for cyanide is presented in Table 17-4 of the TDD as well, and are applicable to those wastewaters from Subcategories A and C operations known or believed to contain cyanide. Compliance monitoring for cyanide should occur in-plant, prior to dilution or mixing with any non-cyanide bearing wastewater. In-plant monitoring is required to prevent compliance through dilution with non-cyanide bearing wastewaters.

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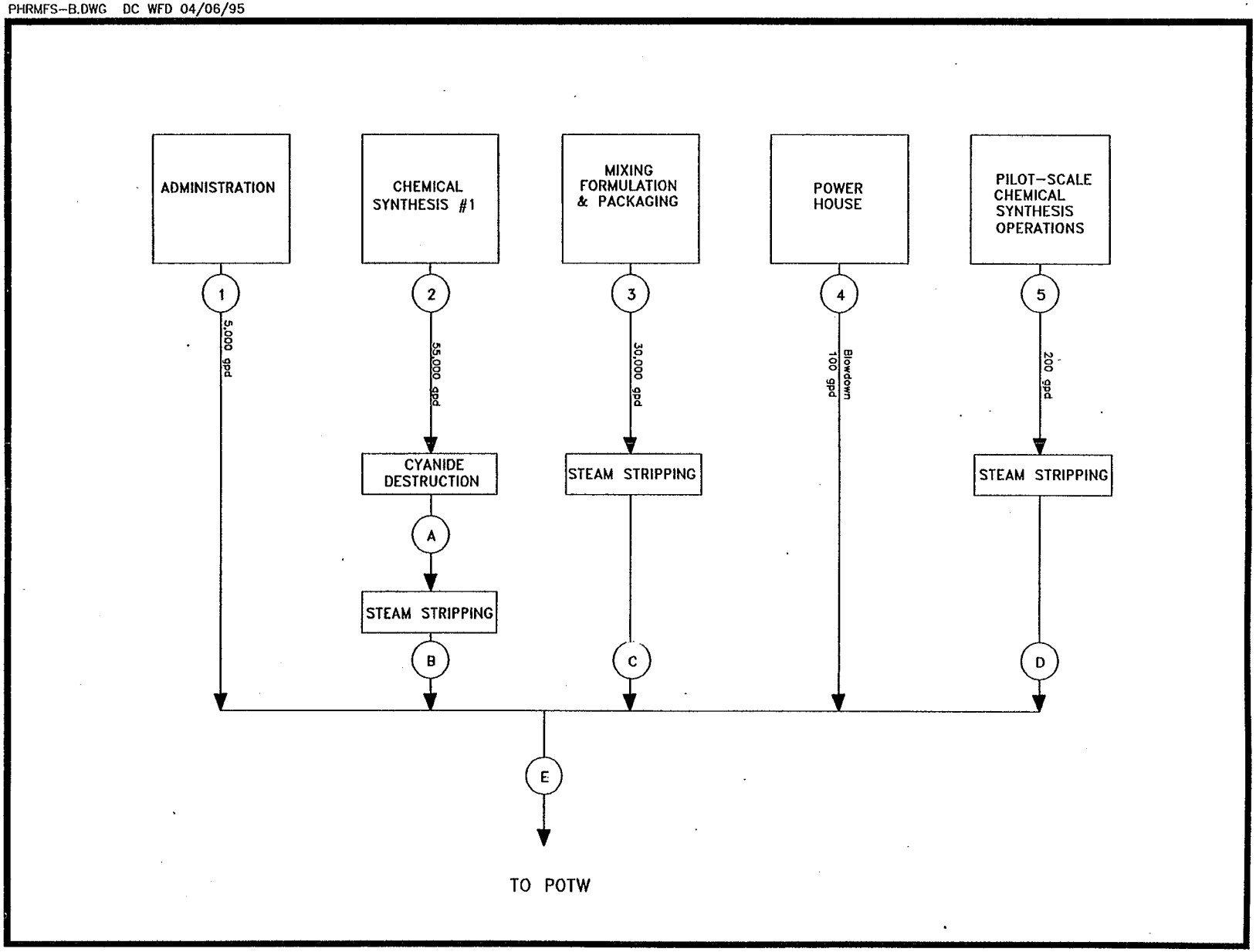

Figure A-2. Flow Schematic for Facility B.

The first step in establishing permit limitations is to determine the types of wastestreams (i.e., regulated process, unregulated process, and dilute). The flow breakdown for Facility B would look like this:

Waste Stream	Flow (gal/day)	
1. Administration	5,000	(Dilute)
2. Chemical synthesis	55,000	(Regulated, Sub. C)
3. Mixing, Formulating, and Packaging	30,000	(Regulated, Sub. D)
4. Boiler Blowdown	100	(Dilute)
5. Pilot-Scale Chemical Synthesis	200	(Regulated, Sub. C)
Total Wastewater Flow:	90,300	
Total Regulated Process:	85,200	
Total Unregulated Process:	0	
Total Dilute:	5,100	

Streams 2, 3, and 5 are considered regulated process wastestreams because effluent limitations have been established for chemical synthesis operations (Subcategory C) and mixing, formulating, and packaging operations (Subcategory D). Note for this example that in the proposed regulation pilot-scale chemical synthesis wastewaters are regulated as normal manufacturing process wastewater, not as research (Subcategory E) wastewater.

We will assume that Facility B has provided the permit writer with an accurate characterization of its process wastestreams by means available such as evaluation of solvent use and disposition data, and has performed analytical scans of each stream. Permit limitations should be established and compliance monitoring required for each regulated pollutant listed on Table 17-2 generated or used at a pharmaceutical manufacturing facility. Limitations and routine compliance monitoring are not required for regulated pollutants not generated or used at a facility. A determination that

regulated pollutants are not generated or used should be based on a review of all raw materials used and an assessment of all chemical processes used, considering resulting products and by-products. The determination that a regulated pollutant is not generated or used must be confirmed by annual chemical analyses of wastewater from each monitoring location. Such confirmation is provided by an analytical measurement of a non-detect value.

The following presents a summary of regulated pollutants found in this facility's wastestreams:

Stream	Subcategory	Flow (gpd)	Pollutant
1	N/A	5,000	No PSES pollutants
2	C	55,000	Acetone, chloroform, toluene, cyanide
3	D	30,000	Acetone, isopropanol, toluene
4	N/A	100	No PSES pollutants
5	C	200	Chloroform, toluene

Based on the above data, permit limitations are established for acetone, chloroform, cyanide, isopropanol, and toluene. All of these pollutants are listed in Table 17-4 of the TDD.

3.2.1 PSES Maximum Limitations for Any One Day

The limitations for both chloroform and toluene would be applied to process wastewater streams 2, 3, and 5, at in-plant location points B, C, and D, prior to any dilution, commingling with other treated wastestreams, and any equalization or treatment units which are open to the atmosphere. (These monitoring points are shown at in-plant

locations after steam stripping. Although steam stripping is the basis for the regulated concentrations, it does not have to be the technology used at the facility.) These maximum daily limitations would be concentration-based, and are ND and 198 μg/L (from Table 17-4) for chloroform and toluene, respectively. Non-detect (ND) values are concentration-based measurements reported below the minimum level that can be reliably measured by the analytical method for the pollutant. Therefore, the permit limitation for chloroform should specify ND for all measurements. Any concentration measurements greater than the ND value for the pollutant are considered out of compliance.

PSES effluent limitations for cyanide should also be applied in-plant. The cyanide standards are applicable to wastewaters from Subcategories A and C operations that contain cyanide. Therefore, the concentration-based limitations for cyanide will apply to process wastestream 2 at point A prior to dilution or mixing with any non-cyanide bearing wastewater. The maximum daily limitation for cyanide is 766 μg/L (from Table 17-4).

The limitations for both acetone and isopropanol would be applied at end-of-pipe location point E.

The total maximum allowable discharge for acetone for any one day can be calculated by determining the mass discharge allowance using the combined wastestream formula (CWF) shown below:

$$M_T = \left[\sum_{i=1}^{N} M_i\right] \times \left[\frac{F_T - F_D}{\sum_{i=1}^{N} F_i}\right]$$

where:

M_T	=	Alternative mass limit for the pollutant in the combined wastestream (mass per day).
M_i	=	Pretreatment standard for the pollutant in the regulated stream i (mass per day)
F_i	=	Average daily flow (at least 30 day average) of the regulated stream i
F_D	=	Average daily flow (at least 30 day average) of dilute wastestream(s) entering the combined treatment system
F_T	=	Average daily flow (at least 30 day average) through the combined treatment facility (including regulated, unregulated, and dilute wastestreams)
N	=	Total Number of regulated streams

In this example, the previously listed variables are calculated as follows:

M_1 = M_4 = 0 (since these streams are considered dilution water)
M_2 = Mass limit for acetone in stream 2
M_2 = 31,400 μg/L × 55,000 gpd × 8.345 × 10^{-9} = 14.4 lbs/day acetone
M_3 = Mass limit for acetone in stream 3
M_3 = 31,400 μg/L × 30,000 gpd × 8.345 × 10^{-9} = 7.86 lbs/day acetone
M_5 = Mass limit for acetone in stream 5
M_5 = 31,400 μg/L × 200 gpd × 8.345 × 10^{-9} = 0.05 lbs/day acetone
F_T = Total flow = 90,300 gpd
F_D = Dilution flow = F_1 + F_4 = 5,1000 gpd
F_2 = Flow in stream 2 = 55,000 gpd
F_3 = Flow in stream 3 = 30,000 gpd
F_5 = Flow in stream 5 = 200 gpd

$$M_T = \frac{22.31 \text{ lbs}}{\text{day}} \times \left[\frac{90{,}300 \text{ gpd} - 5{,}100 \text{ gpd}}{85{,}200 \text{ gpd}} \right] = \frac{22.31 \text{ lbs}}{\text{day}} \text{ acetone}$$

Total facility maximum discharge of acetone for any one day = 22.31 lbs/day.

Maximum day effluent limitations for isopropanol can be calculated in a similar manner.

3.2.2 PSES Monthly Average Limitations for Organic Pollutants

The monthly average discharge limitations for chloroform and toluene are ND and 148 μg/L, respectively. These limitations would be applied to process wastewater streams 2, 3, and 5 at in-plant location points A, B, and C, prior to any dilution, commingling with other treated wastestreams, and any equalization or treatment units which are open to the atmosphere.

The monthly average discharge standard for cyanide is 406 μg/L. This standard will be applied to process wastestream 2 at point A prior to dilution or mixing with any non-cyanide bearing wastewater.

The monthly average discharges for acetone and isopropanol can be calculated by determining the mass discharge allowance using the CWF presented in Section 3.2.1.

To determine the monthly average limitations for acetone, the variables listed in Section 3.2.1 are calculated as follows:

M_1 = M_4 = 0 (since these streams are considered dilution water)
M_2 = Mass limit for acetone in stream 2
M_2 = 9,690 μg/L $\times$ 55,000 gal/day $\times$ 8.345 $\times$ 10^{-9} = 4.45 lbs/day acetone
M_3 = Mass limit for acetone in stream 3
M_3 = 9,690 μg/L $\times$ 30,000 gal/day $\times$ 8.345 $\times$ 10^{-9} = 2.43 lbs/day acetone
M_5 = Mass limit for acetone in stream 5
M_5 = 9,690 μg/L $\times$ 200 gal/day $\times$ 8.345 $\times$ 10^{-9} = 0.02 lbs/day acetone
F_T = Total flow = 90,300 gpd
F_D = Dilution flow = F_1 + F_4 = 5,1000 gpd
F_2 = Flow in stream 2 = 55,000 gpd
F_3 = Flow in stream 3 = 30,000 gpd
F_5 = Flow in stream 5 = 200 gpd

$$M_T = \frac{6.90 \text{ lbs}}{\text{day}} \times \left[\frac{90{,}300 \text{ gpd} - 5{,}100 \text{ gpd}}{85{,}200 \text{ gpd}} \right] = \frac{6.90 \text{ lbs}}{\text{day}} \text{ acetone}$$

The monthly average discharge limitation for acetone is 6.90 lbs/day. Monthly average limitations for isopropanol can be calculated in a similar manner.

3.3 PSES Effluent Limitations for Co-Proposal 2

Co-proposal 2 sets in-plant limitations for the 13 pollutants listed in Table 17-5 of the TDD. There are not end-of-pipe standards for any pollutants under this co-proposal except ammonia. Facility B would have no limitations for acetone and isopropanol under this co-proposal, but would still have in-plant limitations for chloroform, cyanide, and toluene. The limitations for chloroform, cyanide, and toluene would be the same as those shown for co-proposal 1.

4.0 CASE STUDY 3, NSPS FOR A MULTIPLE SUBCATEGORY FACILITY

Facility C is a multiple subcategory direct discharging pharmaceutical facility built after this rule is promulgated and in effect. A wastewater flow schematic for this facility is presented in Figure A-3.

4.1 NSPS Effluent Limitations

Tables 16-2 and 16-3 of the TDD present the proposed daily maximum and monthly average NSPS for Subcategories A and C, and Subcategories B and D, respectively. NSPS for ammonia and the organic pollutants listed in these tables are applicable to the final effluent discharged to the waters of the United States.

The proposed standards are concentration-based and, as such, do not regulate wastewater flow. The permit writer must use a reasonable estimate of process wastewater discharge flow and the concentration-based standards to develop mass-based standards for the NPDES permit.

NSPS for cyanide is presented in Table 16-2 of the TDD as well, and are applicable to those wastewaters from Subcategories A and C operations known or believed to contain cyanide. Compliance monitoring for cyanide should occur in-plant, prior to dilution or mixing with any non-cyanide bearing wastewater. In-plant monitoring is required to prevent compliance through dilution with non-cyanide-bearing wastewaters.

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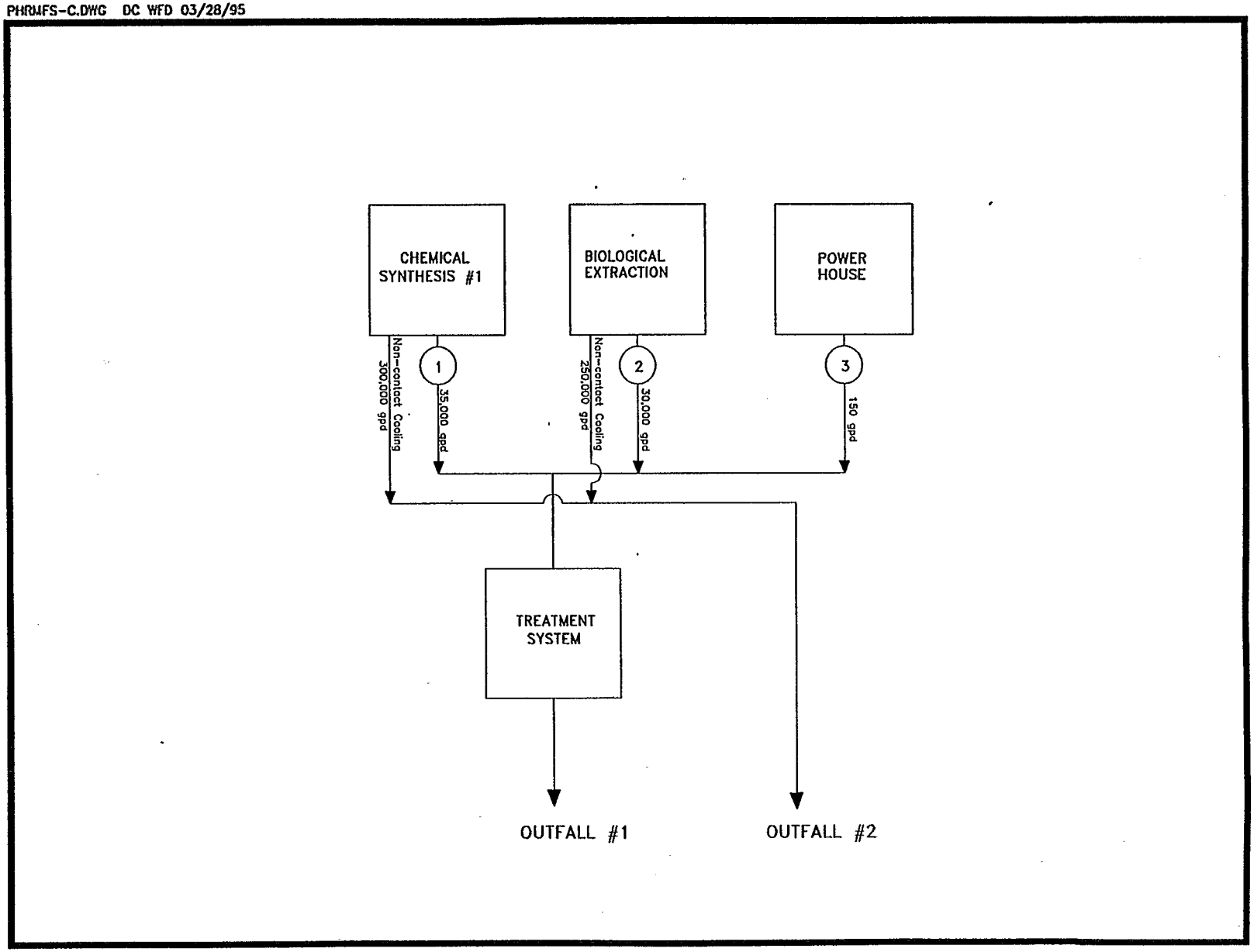

Figure A–3. Flow Schematic for Facility C.

The first step in establishing permit limitations is to determine the types of wastestreams (i.e., regulated process, unregulated process, and dilute). The flow breakdown for Facility C would look like this:

Waste Stream	Flow (gal/day)	
Outfall #001		
1. Chemical Synthesis	35,000	(Regulated, Sub. C)
2. Biological Extraction	30,000	(Regulated, Sub. B)
3. Boiler Blowdown	150	(Dilute)
Total Wastewater Flow:	65,150	
Total Regulated Process:	65,000	
Total Unregulated Process:	0	
Total Dilute:	150	
Outfall #002		
1. Non-Contact Cooling	550,000	
Total Wastewater Flow:	550,000	
Total Regulated Process:	0	
Total Unregulated Process:	0	
Total Dilute:	550,000	

Streams 1 and 2 are considered regulated wastestreams because effluent limitations have been established for chemical synthesis operations (Subcategory C) and biological extraction operations (Subcategory B).

We will assume that Facility C has provided the permit writer with accurate characterization of its process wastestreams by means available such as projected solvent use and disposition data, and analytical scans of each stream. Permit limitations should be established and compliance monitoring required for each regulated pollutant listed on Table 16-1 generated or used at a pharmaceutical manufacturing facility. Limitations

and routine compliance monitoring are not required for regulated pollutants not generated or used at a facility. A determination that regulated pollutants are not generated or used should be based on a review of all raw materials used and an assessment of all chemical processes used, considering resulting products and by-products. The determination that a regulated pollutant is not generated or used must be confirmed by annual chemical analyses of wastewater from each monitoring location. Such confirmation is provided by an analytical measurement of a non-detect value.

The following presents a summary of the regulated pollutants expected to be found in this facility's wastestream:

Stream	Subcategory	Flow (gpd)	Pollutant
1	C	35,000	Methylene chloride, tetrahydrofuran, acetone, methanol, toluene, BOD_5, COD, TSS
2	B	30,000	Methanol, tetrahydrofuran, BOD_5, COD, TSS
3	N/A	150	No NSPS pollutants

Based on the above data, permit writers would use reasonable estimates of the process wastewater discharge flow and the concentration-based standards in Tables 16-2 and 16-3 to develop limitations for methylene chloride, tetrahydrofuran, acetone, methanol, and toluene in the NPDES permit. Permit limitations would also be established for BOD_5, COD, and TSS.

4.2 NSPS Maximum Limitations for Any One Day

As shown in Tables 16-2 and 16-3, methylene chloride, acetone, methanol, and toluene have maximum daily limitations of ND for all subcategories. Non-detect (ND) values are concentration-based measurements reported below the minimum level that can be reliably measured by the analytical method for the pollutant. Therefore, the permit limitation for methylene chloride, acetone, methanol, and toluene should specify ND for all measurements. Any concentration measurements greater than the ND value for the pollutant are considered out of compliance.

Tetrahydrofuran has a numerical limitation for all subcategories. The concentration-based limitations in Tables 16-2 and 16-3 should be converted to maximum daily mass-based limitations as shown below:

Stream 1 (Sub. C): $(910\ \mu g/L \times 35{,}000\ gal/day \times 8.345 \times 10^{-9}) = 0.27\ lbs/day$
Stream 2 (Sub. B): $(910\ \mu g/L \times 30{,}000\ gal/day \times 8.345 \times 10^{-9}) = 0.23\ lbs/day$

Total = 0.50 lbs/day

Stream 3 is considered a dilution stream, and therefore does not receive a discharge mass allowance. The total facility maximum day discharge limitation for tetrahydrofuran is 0.50 lbs/day.

The limitations for BOD_5, COD, and TSS would also be applied to the final effluent. The total NSPS maximum for any one day discharge for BOD_5 can be calculated by summing the allowable mass discharges for each process stream as follows:

Stream 1 (Sub. C): $(62\ mg/L \times 35{,}000\ gal/day \times 7.345 \times 10^{-6}) = 18.1\ lbs/day$
Stream 2 (Sub. B): $(34\ mg/L \times 30{,}000\ gal/day \times 7.345 \times 10^{-6}) = 8.5\ lbs/day$

Total = 26.6 lbs/day BOD_5

The total facility maximum discharge of BOD_5 for any one day is 26.6 lbs/day. Maximum day effluent limitations for COD and TSS can be calculated in a similar manner.

4.3 NSPS Monthly Average Limitations

Maximum for any one day and monthly average limitations for methylene chloride, acetone, methanol, and toluene are ND. Therefore, the permit limitations for these pollutants should specify ND for all measurements.

The total NSPS monthly average discharge limitation for tetrahydrofuran can be calculated as shown below.

Stream 1 (Sub. C): $(264\ \mu g/L \times 35{,}000\ gal/day \times 8.345 \times 10^{-9}) = 0.08$ lbs/day
Stream 2 (Sub. B): $(264\ \mu g/L \times 30{,}000\ gal/day \times 8.345 \times 10^{-9}) = 0.07$ lbs/day

Total = 0.15 lbs/day

Stream 3 is considered a dilution stream, and therefore does not receive a discharge mass allowance. The monthly average discharge limitation for tetrahydrofuran is 0.15 lbs/day.

The total NSPS monthly average discharge limitation for BOD_5 can be calculated as follows:

Stream 1 (Sub. C): $(29\ mg/L \times 35{,}000\ gal/day \times 8.345 \times 10^{-6}) = 8.47$ lbs/day
Stream 2 (Sub. B): $(10\ mg/L \times 30{,}000\ gal/day \times 8.345 \times 10^{-6}) = 2.50$ lbs/day

Total = 11.0 lbs/day BOD_5

The monthly average discharge limitation for BOD_5 is 11.0 lbs/day. Monthly average effluent limitations for COD and TSS can be calculated in a similar manner.

5.0 CASE STUDY 4, PSNS FOR A MULTIPLE SUBCATEGORY FACILITY

Facility D is a multiple subcategory indirect discharging pharmaceutical facility built after this rule is promulgated and in effect. A wastewater flow schematic for this facility is presented in Figure A-4.

5.1 PSNS Effluent Limitations

Two scenarios are presented for PSNS. The first would apply under co-proposal 1 and the second would apply under co-proposal 2. Co-proposal 1 for Subcategories A and C sets in-plant standards for 28 pollutants and end-of-pipe standards for 19 pollutants. Co-proposal 2 for Subcategories A and C sets in-plant standards for 13 pollutants, but has no end-of-pipe standards except for ammonia. In Subcategories B and D cyanide and ammonia are not regulated. Co-proposal 1 for Subcategories B and D sets in-plant standards for 27 pollutants and end-of-pipe standards for 18 pollutants. Co-proposal 2 for Subcategories B and D sets in-plant standards for 12 pollutants.

5.2 PSNS Effluent Limitations for Co-Proposal 1

Table 17-6 of the TDD presents the proposed daily maximum and monthly average PSNS for Subcategories A, B, C, and D. The proposed standards are concentration-based and, as such, do not regulate wastewater flow. Organics being controlled under PSNS have been divided into two groups, one list for organics to be controlled in-plant, and a second list of less volatile organics that are controlled at the end-of-pipe.

PSNS for cyanide is presented in Table 17-6 of the TDD as well, and are applicable to those wastewaters from Subcategories A and C operations known or believed to contain cyanide. Compliance monitoring for cyanide should occur in-plant, prior to dilution or mixing with any non-cyanide bearing wastewater. In-plant monitoring is required to prevent compliance through dilution with non-cyanide bearing wastewaters.

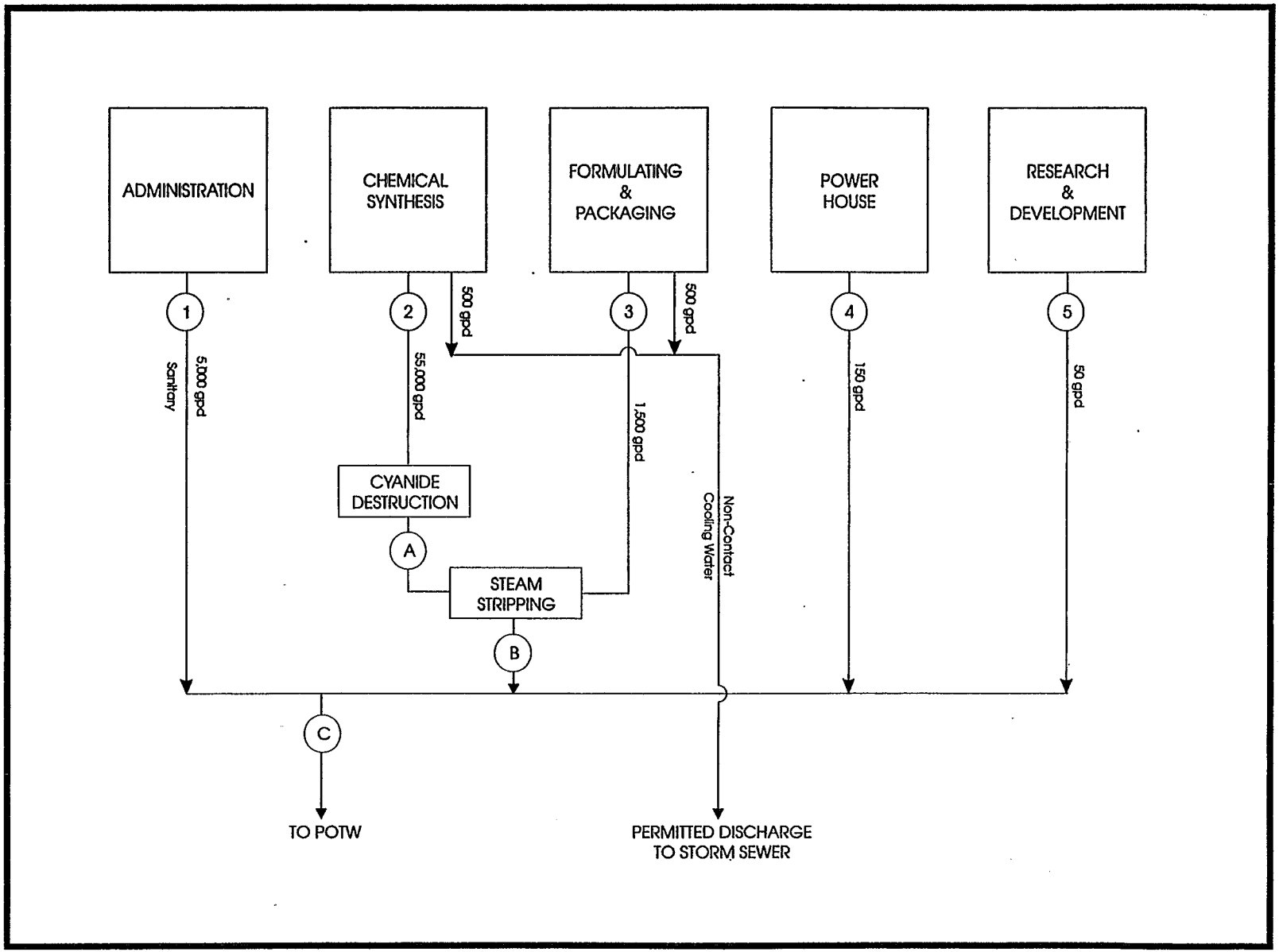

Figure A-4. Flow Schematic for Facility D.

The first step in establishing permit limitations is to determine the types of wastestreams (i.e., regulated process, unregulated process, and dilute). The flow breakdown for Facility D would look like this:

Waste Stream	Flow (gal/day)	
Outfall #001		
1. Administration (Sanitary)	5,000	(Dilute)
2. Chemical Synthesis #1	55,000	(Regulated, Sub. C)
3. Mixing, Formulating, and Packaging	1,500	(Regulated, Sub. D)
4. Boiler Blowdown	150	(Dilute)
5. Research and Development	50	(Unregulated, Sub. E)
Total Wastewater Flow:	61,700	
Total Regulated Process:	56,500	
Total Unregulated Process:	50	
Total Dilute:	5,150	
Outfall #002		
1. Non-Contact Cooling	1,000	
Total Wastewater Flow:	1,000	
Total Regulated Process:	0	
Total Unregulated Process:	0	
Total Dilute:	1,000	

Streams 2 and 3 are considered regulated process wastestreams because effluent limitations have been established for chemical synthesis operations (Subcategory C) and mixing, compounding and formulating operations (Subcategory D). Thus, a reasonable estimate of the process wastewater discharge flow for this example facility is 56,500 gal/day.

Stream 5 is considered an unregulated process wastestream because effluent limitations for organic pollutants have not been established for research and development operations (Subcategory E).

We will assume that Facility D has provided the permit writer with accurate characterization of its process wastestreams by means available such as projected solvent use and disposition data, and analytical scans of each stream. Permit limitations should be established and compliance monitoring required for each regulated pollutant listed on Table 17-2 generated or used at a pharmaceutical manufacturing facility. Limitations and routine compliance monitoring are not required for regulated pollutants not generated or used at a facility. A determination that regulated pollutants are not generated or used should be based on a review of all raw materials used and an assessment of all chemical processes used, considering resulting products and by-products. The determination that a regulated pollutant is not generated or used must be confirmed by annual chemical analyses of wastewater from each monitoring location. Such confirmation is provided by an analytical measurement of a non-detect value.

The following presents a summary of the regulated pollutants expected to be found in this facility's wastestreams:

Stream	Subcategory	Flow (gpd)	Pollutant
1	N/A	5,000	No PSNS pollutants
2	C	55,000	Methylene chloride, tetrahydrofuran, ammonia, methanol, cyanide
3	D	1,500	Methanol, tetrahydrofuran
4	N/A	150	No PSNS pollutants
5	E	50	Ammonia

Based on the above data, permit limitations are established for methylene chloride, tetrahydrofuran, ammonia, methanol, and cyanide. All of these pollutants are listed in Table 17-6.

5.2.1 PSNS Maximum Limitations for Any One Day

The limitations for both methanol and methylene chloride would be applied at in-plant location point B, prior to any dilution, commingling with other treated wastestreams, and any equalization or treatment units which are open to the atmosphere. In this example, they would be applied to wastestreams 2 and 3. These maximum daily limitations would be concentration-based, and are 8,320 μg/L and 809 μg/L (from Table 17-6) for methanol and methylene chloride, respectively. In-plant monitoring is required to prevent compliance through dilution and by cross-media transfer of these pollutants from wastewater to the atmosphere during collection, equalization, and end-of-pipe biological treatment.

PSNS effluent limitations for cyanide should also be applied in-plant. The cyanide standards are applicable to wastewaters from Subcategories A and C operations that contain cyanide. Therefore, the concentration-based limitations for cyanide will apply to process wastestream 2 at point A, prior to dilution or mixing with any non-cyanide bearing wastewater. The maximum daily limitation for cyanide is 766 μg/L (from Table 17-6).

PSNS for ammonia and tetrahydrofuran would be applied to the facility effluent at point C. The concentration-based standards contained in Table 17-6 would be converted to mass-based

permit limitations. These mass-based limitations can be calculated using the CWF shown below:

$$M_T = \left[\sum_{i=1}^{N} M_i\right] \times \left[\frac{F_T - F_D}{\sum_{i=1}^{N} F_i}\right]$$

where:

M_T	=	Alternative mass limit for the pollutant in the combined wastestream (mass per day)
M_i	=	Pretreatment standard for the pollutant in the regulated stream i (mass per day)
F_i	=	Average daily flow (at least 30 day average) of the regulated stream i
F_D	=	Average daily flow (at least 30 day average) of dilute wastestream(s) entering the combined treatment system
F_t	=	Average daily flow (at least 30 day average) through the combined treatment facility (including regulated, unregulated, and dilute wastestreams)
N	=	Total number of regulated streams

To determine the mass-based limitation for ammonia, the previously listed variables are calculated as follows:

$M_1 = M_3 = M_4 = M_5 = 0$ (since these streams are considered either dilution water, or unregulated process wastewater with respect to ammonia)

M_2 = Mass limit for ammonia in stream 2

M_2 = 12,900 μg/L $\times$ 55,000 gal/day $\times$ 8.345 $\times$ 10^{-9} = 5.92 lbs/day ammonia

Wastestream 1 (sanitary wastewater) and wastestream 4 (boiler blowdown) are considered dilution water. Wastestream 3 (wastewater from formulating and packaging, Subcategory D) is also considered dilution water for the purpose of calculating ammonia limitations, because ammonia is not regulated in Subcategory D, and ammonia is not present in wastestream 3 at this facility. Wastestream 5 (wastewater from research operations, Subcategory E) is considered unregulated process wastewater, because the

facility has made a demonstration (based on analysis of wastewater samples) that ammonia is expected to be present in this wastewater at treatable concentrations. Therefore:

F_T = Total flow = 61,700 gpd
F_D = Dilution flow = $F_1 + F_3 + F_4$ = 6,650 gpd
F_2 = 55,000 gpd

$$M_T = \frac{5.92 \text{ lbs}}{\text{day}} \times \left[\frac{61{,}700 \text{ gpd} - 6{,}650 \text{ gpd}}{55{,}000 \text{ gpd}}\right] = \frac{5.93 \text{ lbs}}{\text{day}} \text{ ammonia}$$

To determine the mass-based limitation for tetrahydrofuran, the previously listed variables are calculated as follows:

M_1 = M_4 = 0 (since these streams are considered dilution water)
M_2 = Mass limit for tetrahydrofuran in Stream 2
M_2 = 9,210 μg/L × 55,000 gal/day × 8.345 × 10^{-9} = 4.23 lbs/day
M_3 = Mass limit for tetrahydrofuran in stream 3
M_3 = 9,210 μg/L × 1,500 gal/day × 8.345 × 10^{-9} = 0.12 lbs/day
M_5 = 0 (since this wastestream is unregulated)

While Subcategory E wastewater is unregulated for the pollutant tetrahydrofuran according to the definition in the General Pretreatment Regulations, Control Authorities have the authority to determine whether unregulated streams should be considered dilution under 40 CFR § 403.6(d). Since tetrahydrofuran was not found to be present in Subcategory E wastewater in this example, this wastestream is considered here as dilution water.

F_T = Total flow = 61,700 gpd
F_D = Dilution flow = $F_1 + F_4 + F_5$ = 5,200 gpd
F_2 = 55,000 gpd
F_3 = 1,500 gpd

$$M_T = \frac{4.35 \text{ lbs}}{\text{day}} \times \left[\frac{61{,}700 \text{ gpd} - 5{,}200 \text{ gpd}}{56{,}500 \text{ gpd}}\right] = 4.35 \text{ lbs/day tetrahydrofuran}$$

Total facility maximum day discharge limitations for ammonia and tetrahydrofuran are 5.93 lbs/day and 4.35 lbs/day, respectively.

5.2.2 PSNS Monthly Average Limitations

The monthly average discharge standards for methanol and methylene chloride are ND and 279 μg/L, respectively. These standards would be applied to process wastewater streams 2 and 3 at point B, prior to any dilution, commingling with other treated wastestreams, and any equalization or treatment units which are open to the atmosphere. Note that the published monthly average standard for methanol is ND. However, since the maximum for any one day standard is not ND, measurements above the minimum level are permitted. Within the course of a month, the average value of all measurements should be equal to or less than the minimum level of 3,180 μg/L.

The monthly average discharge standard for cyanide is 406 μg/L. This standard will be applied to process wastestream 2 at point A, prior to dilution or mixing with any non-cyanide bearing wastewater.

The monthly average discharges for ammonia and tetrahydrofuran should be applied at end-of-pipe location point C and can be calculated by using the CWF shown in Section 5.2.1 of this example. The following variables would be calculated to determine the ammonia monthly average discharge limitation.

$M_1 = M_3 = M_4 = M_5 = 0$

M_2 = 10,900 μg/L $\times$ 55,000 gal/day $\times$ 8.345 $\times$ 10^{-9} = 5.00 lbs/day ammonia

F_T = Total flow = 61,700 gpd

F_D = Dilution flow = $F_1 + F_3 + F_4$ = 6,650 gpd

F_2 = 55,000 gpd

$$M_T = \frac{5.00 \text{ lbs}}{\text{day}} \times \left[\frac{61{,}700 \text{ gpd} - 6{,}650 \text{ gpd}}{55{,}000 \text{ gpd}} \right] = \frac{5.00 \text{ lbs}}{\text{day}} \text{ ammonia}$$

The monthly average for tetrahydrofuran is calculated similarly and is shown below:

$M_1 = M_4 = M_5 = 0$

M_2 = 3,360 μg/L × 55,000 gal/day × 8.345 × 10^{-9} = 1.54 lbs/day tetrahydrofuran

M_3 = 3,360 μg/L × 1,500 gal/day × 8.345 × 10^{-9} = 0.042 lbs/day tetrahydrofuran

F_T = 61,700 gpd

F_D = $F_1 + F_4 + F_5$ = 5,200 gpd

F_2 = 55,000 gpd

F_3 = 1,500 gpd

$$M_T = \frac{1.58 \text{ lbs}}{\text{day}} \times \left[\frac{61{,}700 \text{ gpd} - 5{,}200 \text{ gpd}}{56{,}500 \text{ gpd}} \right] = \frac{1.58 \text{ lbs}}{\text{day}} \text{ tetrahydrofuran}$$

The monthly average discharge limitations for ammonia and tetrahydrofuran are 5.00 lbs/day and 1.58 lbs/day, respectively.

5.3 PSNS Effluent Limitations for Co-Proposal 2

Co-proposal 2 sets in-plant limitations for the 13 pollutants listed in Table 17-7 of the TDD. There are no end-of-pipe limitations for any pollutants except ammonia under this co-proposal. Facility D would have no limitations for methanol and tetrahydrofuran under this co-proposal, but would still have in-plant limitations for cyanide and methylene chloride, and an end-of-pipe limitation for ammonia. The limitations for these three pollutants would be the same as those shown for co-proposal 1.

6.0 CASE STUDY 5, BPT AND BAT EFFLUENT LIMITATIONS FOR A MULTIPLE INDUSTRIAL CATEGORY FACILITY

Facility E is a direct discharging manufacturing facility with operations in two industrial categories. Pharmaceuticals as well as bulk organic chemicals are produced at this facility. A wastewater flow schematic for this facility is presented in Figure A-5.

6.1 BPT Effluent Limitations

The revised BPT effluent limitations guidelines establish new BOD_5, COD, and TSS effluent limitations for Subcategory A, B, C, and D direct discharging facilities. As described in Case Study 1, the pH effluent limit will not be amended, and other conventional pollutants will not be regulated by BPT for the pharmaceutical manufacturing point source category.

The proposed effluent limitations and guidelines are concentration-based and, as such, do not regulate wastewater flow. The permit writer must use a reasonable estimate of process wastewater discharge flow and the concentration-based limitations to develop mass-based limitations for the NPDES permit. Table 13-1 of the TDD presents the proposed maximum daily and monthly average BPT effluent limitations for Subcategory A, B, C, and D direct discharging facilities.

The limitations for BOD_5, COD, and TSS will be applied to the final effluent at monitoring point B. An example calculation of the BPT maximum day and monthly average BOD_5, COD, and TSS limitations for this facility is as follows.

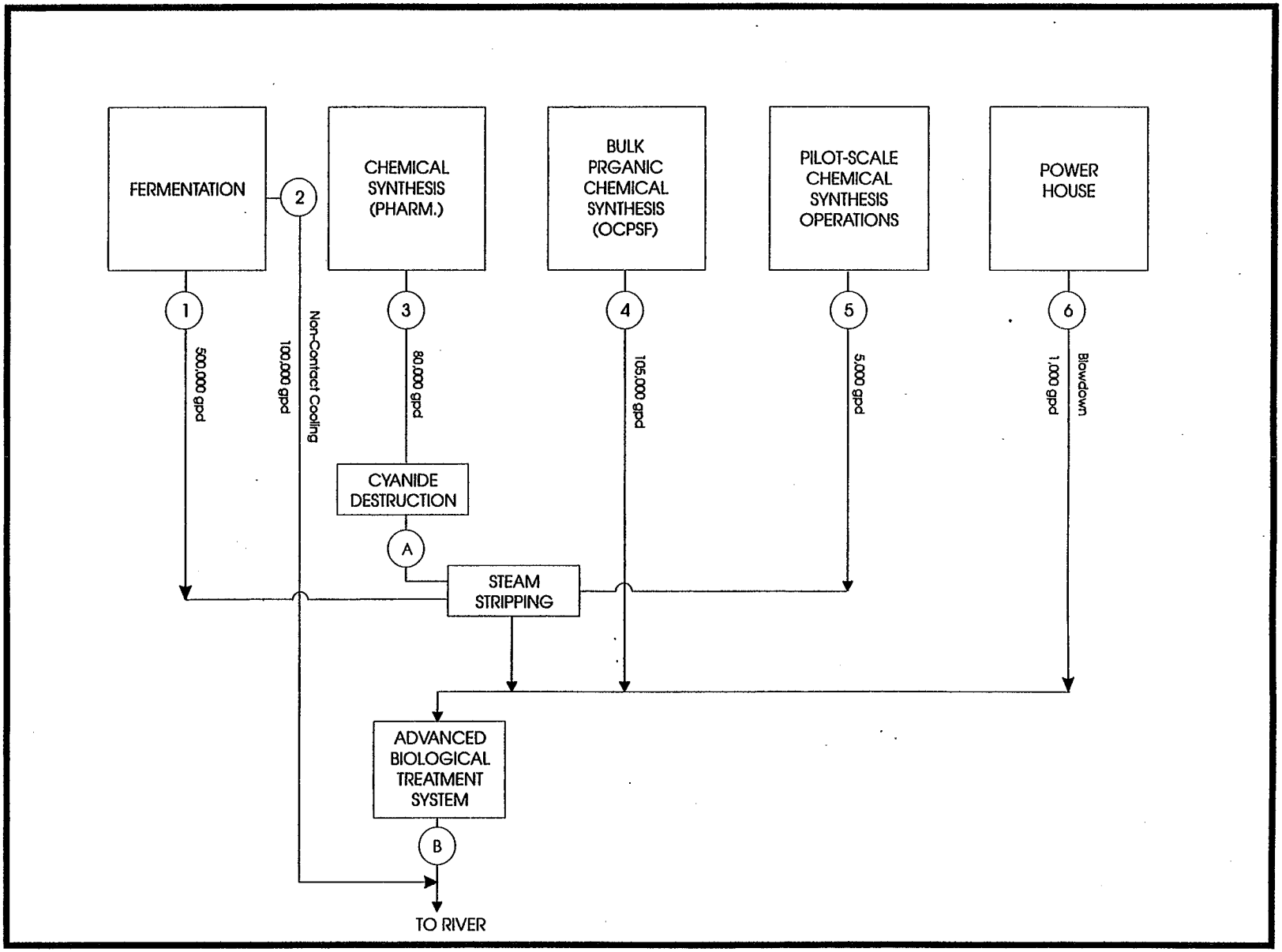

Figure A-5. Flow Schematic for Facility E.

6.1.1 Maximum Effluent Limitations for Any One Day

The first step in establishing permit limitations is to determine the types of wastestreams present. The flow breakdown for facility E would look like this:

Waste Stream	Flow (gal/day)	
1. Fermentation	500,000	(Regulated, Sub. A)
3. Chemical Synthesis	80,000	(Regulated, Sub. C)
4. Bulk Organic Chemicals	105,000	(Regulated, OCPSF)
5. Chemical Synthesis	5,000	(Regulated, Sub. C)
6. Boiler Blowdown	1,000	(Dilute)
Total Wastewater Flow:	691,000	
Total Regulated Process:	690,000	
Total Unregulated Process:	0	
Total Dilute:	1,000	
2. Noncontact Cooling Water (added after monitoring point B)	100,000	(Dilute)

Streams 1, 3, 4, and 5 are considered regulated wastestreams as effluent limitations have been established for fermentation operations (Subcategory A), chemical synthesis operations (Subcategory C), and OCPSF bulk organic chemical operations. (3)

Table 13-1 of the TDD presents the proposed maximum daily and monthly average BPT effluent limitations for Subcategories A and C. 40 CFR §414.71 presents the proposed maximum daily and monthly average BPT effluent limitations for bulk organic chemical OCPSF wastewaters. (3) The total BPT maximum for any one day discharge for BOD_5 can be calculated as follows:

Stream 1 (Sub. A): (139.7 mg/L × 500,000 gal/day × 8.345 × 10^{-6}) = 582.9 lbs/day
Stream 3 (Sub. C): (139.7 mg/L × 80,000 gal/day × 8.345 × 10^{-6}) = 93.3 lbs/day
Stream 4 (OCPSF): (92 mg/L × 105,000 gal/day × 8.345 × 10^{-6}) = 80.6 lbs/day
Stream 5 (Sub. C): (139.7 mg/L × 5,000 gal/day × 8.345 × 10^{-6}) = 5.8 lbs/day

Total = 763 lbs BOD_5/day

TSS maximum day effluent limitations can be calculated in a similar manner.

Proposed maximum daily and monthly average COD effluent limitations for Subcategories A and C are also presented in Table 13-1. However, COD is not regulated in wastewater from chemical synthesis operations at OCPSF facilities. (3) In cases where OCPSF wastewaters are combined with pharmaceutical wastewaters and treated in a central unit, the maximum daily limitation for COD can be calculated by determining the mass discharge allowance using the CWF shown below:

$$M_T = \left[\sum_{i=1}^{N} M_i\right] \times \left[\frac{F_T - F_D}{\sum_{i=1}^{N} F_i}\right]$$

where:

M_T	=	Alternative mass limit for the pollutant in the combined wastestream (mass per day).
M_i	=	Treatment standard for the pollutant in the regulated stream i (mass per day)
F_i	=	Average daily flow (at least 30 day average) of the regulated stream i
F_D	=	Average daily flow (at least 30 day average) of dilute wastestream(s) entering the combined treatment system
F_T	=	Average daily flow (at least 30 day average) through the combined treatment facility (including regulated, unregulated, and dilute wastestreams)
N	=	Total Number of regulated streams

In this example, the previously listed variables are calculated as follows:

$M_2 = M_4 = M_6 = 0$ (since these streams are considered dilution or unregulated process wastewater)

M_1 = Mass limit for COD in stream 1
M_1 = 1,100 mg/l × 500,000 gal/day × 8.345 × 10^{-6} = 4,589.75 lbs/day
M_3 = Mass limit for COD in stream 3
M_3 = 1,100 mg/L × 80,000 gal/day × 8.345 × 10^{-6} = 734.36 lbs/day
M_5 = Mass limit for COD in stream 5
M_5 = 1,100 mg/L × 5,000 gal/day × 8.345 × 10^{-6} = 45.90 lbs/day
F_T = Total flow = 791,000 gpd
F_D = Dilution flow = F_6 = 1,000 gpd
F_1 = Flow in stream 1 = 500,000 gpd
F_3 = Flow in stream 3 = 80,000 gpd
F_5 = Flow in stream 5 = 5,000 gpd

$$M_T = \frac{5{,}370 \text{ lbs}}{\text{day}} \times \left[\frac{691{,}000 \text{ gpd} - 1{,}000 \text{ pgd}}{585{,}000 \text{ gpd}}\right] = 6{,}334 \text{ lbs/day COD}$$

Total facility discharge limitation for any one day for COD is 6,334 lbs/day.

6.1.2 Monthly Average Effluent Limitations

Monthly average limitations for BOD_5 can be calculated as shown below:

Stream 1 (Sub. A): (57.8 mg/L × 500,000 × 8.345 × 10^{-6}) = 241.2 lbs/day
Stream 3 (Sub. C): (57.8 mg/L × 80,000 × 8.345 × 10^{-6}) = 38.6 lbs/day
Stream 4 (OCPSF): (34 mg/L × 105,000 × 8.345 × 10^{-6}) = 29.8 lbs/day
Stream 5 (Sub. C): (57.8 mg/L × 5,000 × 8.345 × 10^{-6}) = 2.4 lbs/day

Total = 312 lbs BOD_5/day

TSS monthly average effluent limitations can be calculated in a similar manner.

The monthly average limitations for COD can be determined by using the CWF from Section 6.1.1. The following variables should be changed from those listed in Section 6.1.1:

M_1 = 628 mg/L × 500,000 gal/day × 8.345 × 10^{-6} = 2,620.33 lbs/day

M_3 = 628 mg/L × 80,000 gal/day × 8.345 × 10^{-6} = 419.25 lbs/day

M_5 = 628 mg/L × 5,000 gal/day × 8.345 × 10^{-6} = 26.20 lbs/day

$$M_T = \frac{3{,}066 \text{ lbs}}{\text{day}} \times \left[\frac{691{,}000 \text{ gpd} - 1{,}000 \text{ gpd}}{585{,}000 \text{ gpd}}\right] = 3{,}616 \text{ lbs/day COD}$$

Total facility monthly average discharge limitation for COD is 3,616 lbs/day.

6.2 BAT Effluent Limitations

Tables 15-2 and 15-3 of the TDD present the proposed maximum daily and monthly average BAT effluent limitations guidelines for Subcategories A and C, and Subcategories B and D, respectively.

We will assume that Facility E has provided the permit writer with an accurate characterization of its process wastestreams by means available such as solvent use and disposition data, and analytical scans of each stream. Permit limitations should be established and compliance monitoring required for each regulated pollutant listed on Table 15-1 generated or used at a pharmaceutical manufacturing facility. Limitations and routine compliance monitoring are not required for regulated pollutants not generated or used at a facility. A determination that regulated pollutants are not generated or used should be based on a review of all raw materials used and an assessment of all chemical processes used, considering resulting products and by-products. The determination that a regulated pollutant is not generated or used must be confirmed by annual chemical analyses of wastewater from each monitoring location. Such confirmation is provided by an analytical measurement of a non-detect value.

The following presents a summary of the regulated pollutants expected to be found in this facility's wastestreams:

Stream	Subcategory	Flow (gal/day)	Pollutant	Concentration (mg/L)
1	A	500,000	Methylene chloride Methanol Toluene	100 1,000 700
2	N/A	100,000	None	None
3	C	80,000	Cyanide Aniline Methylene chloride Methanol	50 500 200 100
4	OCPSF	105,000	Aniline Methylene chloride	100 150
5	C	5,000	Methanol	250
6	N/A	1,000	None	None

Based on the above data, permit limitations would be established for aniline, methanol, methylene chloride, and toluene.

6.2.1 BAT Maximum Limitations for Any One Day

The limitations for all organic pollutants listed would be applied to the final effluent at monitoring point B. The Subcategories A and C maximum daily limitations for methanol are ND (from Table 15-2). Therefore, the permit limitation for methanol is concentration-based and should be ND for all measurements. Non-detect (ND) values are concentration-based measurements reported below the minimum level that can be reliably measured by the analytical method for the pollutant. Therefore, the permit limitation for methanol should specify ND for all measurements. Any concentration measurements greater than the ND value for the pollutant are considered out of compliance.

BAT effluent limitations for cyanide should be applied in-plant. The cyanide standards are applicable to wastewaters from Subcategories A and C operations that contain cyanide. Therefore, the concentration-based limitations for cyanide will apply to process wastestream 3 at point A, prior to dilution or mixing with any non-cyanide bearing wastewater. The maximum daily limitation for cyanide is 766 μg/L (from Table 15-2).

The allowable mass discharge of methylene chloride for any one day can be calculated as follows. Streams 2 and 6 are dilution water in this example.

BAT Maximum Day Effluent Limitation For Methylene Chloride

Methylene chloride is present and regulated in both pharmaceutical and OCPSF bulk chemicals wastewater. We are assuming Facility E produces more than five million pounds of OCPSF chemicals per year, and have applied the methylene chloride daily limitation for OCPSF wastewaters listed in 40 CFR §414.91 as shown below. (3) The limitations for methylene chloride for Subcategories A and C are ND. However, methylene chloride has a numerical limitation for OCPSF regulations. (3) Since monitoring points for organic pollutants under BAT are at end-of-pipe locations and all process wastewaters will be combined at this location, a mass limitation for the combined wastestream can be determined by using the numerical value of the minimum level of this pollutant to determine the Subcategory A and C portion of the mass limitations.

Stream 1 (Sub. A): $(10\ \mu g/L \times 800{,}000 \times 8.345 \times 10^{-9}) = 0.042$ lbs/day
Stream 3 (Sub. C): $(10\ \mu g/L \times 80{,}000 \times 8.345 \times 10^{-9}) = 0.007$ lbs/day
Stream 4 (OCPSF): $(89\ \mu g/L \times 105{,}000 \times 8.345 \times 10^{-9}) = 0.078$ lbs/day
Stream 5 (Sub. C): $(10\ \mu g/L \times 5{,}000 \times 7.345 \times 10^{-9}) = 0.0004$ lbs/day

Total = 0.127 lbs/day

The total maximum day discharge for methylene chloride is 0.127 lbs/day.

BAT Maximum Day Effluent Limitation For Aniline

Aniline is present in streams 3 and 4 but is not regulated in wastewater from chemical synthesis operations at OCPSF facilities (stream 4). In cases where OCPSF wastewaters are combined with pharmaceutical wastewaters and treated as a central unit, the maximum daily limitations for aniline can be calculated by determining the mass discharge allowance using the CWF shown in Section 6.1.1. The following variables should be changed from those listed in Section 6.1.1:

$$M_1 = 10\mu g/L \times 500{,}000 \text{ gal/day} \times 8.345 \times 10^{-9} = 0.042 \text{ lbs/day}$$
$$M_3 = 10\mu g/L \times 80{,}000 \text{ gal/day} \times 8.345 \times 10^{-9} = 0.007 \text{ lbs/day}$$
$$M_5 = 10\mu g/L \times 5{,}000 \text{ gal/day} \times 8.345 \times 10^{-9} = 0.0004 \text{ lbs/day}$$

$$M_T = \frac{0.0494 \text{ lbs}}{\text{day}} \times \left[\frac{691{,}000 \text{ gpd} - 1{,}000 \text{ gpd}}{585{,}000 \text{ gpd}}\right] = 0.058 \text{ lbs/day}$$

The facility maximum discharge limitation for any one day for aniline is 0.0058 lbs/day.

BAT Maximum Day Effluent Limitation for Toluene

The limitations for toluene for Subcategories A and C are ND. However, toluene has a numerical limitation for OCPSF regulations. (3) Since monitoring points for organic pollutants under BAT are at end-of-pipe locations and all process wastewater will be combined at this location, a mass limitation for the combined wastestream can be determined by using the numerical value of the minimum level of this pollutant to determine the Subcategory A and C portion of the mass limitations.

Stream 1 (Sub. A): $(10\ \mu g/L \times 500{,}000 \times 8.345 \times 10^{-9}) = 0.042$ lbs/day
Stream 3 (Sub. C): $(10\ \mu g/L \times 80{,}000 \times 8.345 \times 10^{-9}) = 0.007$ lbs/day
Stream 4 (OCPSF): $(80\ \mu g/L \times 105{,}000 \times 8.345 \times 10^{-9}) = 0.070$ lbs/day
Stream 5 (Sub. C): $(10\ \mu g/L \times 5{,}000 \times 8.345 \times 10^{-9}) = 0.0004$ lbs/day

Total = 0.12 lbs/day toluene
The facility maximum discharge limitation for any one day for toluene is 0.12 lbs/day.

6.2.2 BAT Monthly Average Limitations For Organic Pollutants

Monthly average limitations for methanol are ND, the same as they were for maximum daily limitations. Thus, the permit limitations for methanol should be ND for all measurements.

The monthly average discharge standard for cyanide is 406 μg/L. This standard will be applied to process wastestream 3 at point A, prior to dilution or mixing with any non-cyanide bearing wastewater.

BAT Monthly Average Limitation for Methylene Chloride

The monthly average limitations for methylene chloride can be calculated in the same manner as the daily maximum limitations. These calculations are shown below:

Subcategories A and C allowable discharge:

$10\ \mu g/L \times (500{,}000\ gpd + 80{,}000\ gpd + 5{,}000\ gpd) \times 8.345 \times 10^{-9} = 0.049\ lbs/day$

OCPSF Bulk Chemicals Subcategory:

$40\ \mu g/L \times 105{,}000\ gpd \times 8.345 \times 10^{-9} = 0.035\ lbs/day$

Total = 0.084 lbs/day

The monthly average discharge limitation for methylene chloride is 0.084 lbs/day.

BAT Monthly Average Limitation For Aniline

The monthly limitations for aniline are the same as the daily maximum limitations shown in Section 6.1.2.

BAT Monthly Average Limitation for Toluene

The monthly average limitations for toluene can be calculated in the same manner as the daily maximum limitations. These calculations are shown below:

Subcategories A and C allowable discharge:
10 μg/L $\times$ (500;000 gpd + 80,000 gpd + 5,000 gpd) $\times$ 8.345 $\times$ 10^{-9} = 0.049 lbs/day

OCPSF Bulk Chemicals Subcategory:
26 μg/L $\times$ 105,000 gpd $\times$ 8.345 $\times$ 10^{-9} = 0.023 lbs/day

Total = 0.072 lbs/day toluene

The monthly average discharge limitation for toluene is 0.072 lbs/day.

REFERENCES

1. U.S. EPA, Office of Water. Training Manual for NPDES Permit Writers. EPA 833-B-93-003, U.S. Environmental Protection Agency, Washington, D.C., 1993.

2. U.S. EPA. Pharmaceutical Manufacturing Point Source Category Effluent Limitations Guidelines, Pretreatment Standards, and New Source Performance Standards; Proposed Regulation, 40 CFR Part 439, FRL 2229-3, Federal Register, November 26, 1982.

3. U.S. EPA. Plastics, and Synthetic Fibers Effluent Limitations Guidelines, Pretreatment Standards, and New Source Performance Standards; 40 CFR Part 414.

APPENDIX B
BEST MANAGEMENT PRACTICES
FOR THE
PHARMACEUTICAL MANUFACTURING INDUSTRY

1.0 INTRODUCTION AND BACKGROUND

Section 304(e) of the CWA gives the Administrator the authority to publish regulations, in addition to the effluent limitations guidelines and standards, to control plant site runoff, spillage or leaks, sludge or waste disposal, and drainage from raw material storage that the Administrator determines are associated with or ancillary to the industrial manufacturing or treatment process of the regulated point source category and that she (he) determines may contribute significant amounts of pollutants to waters of the United States.

EPA is not proposing in the proposed rules best management practices (BMPs) pursuant to Section 304(e) of the Clean Water Act. However, EPA is soliciting comment on whether BMPs are applicable to the pharmaceutical industry and, if so, what they should include. See section XIII of the preamble for solicitation of data and comments, solicitation number 31.0. BMPs established under Section 304(e) may be different from effluent limitations guidelines and standards principally because BMPs are specific requirements for conduct, not performance standards.

When EPA sets technology-based effluent limits, those limits may be achieved by any technology a discharger chooses. However, when EPA establishes BMPs under Section 304(e) of the CWA, and those BMPs are incorporated into a discharger's permit, the discharger must perform those specific BMPs. The fact that a discharger had met all its technology-based effluent limits would not be a defense, if the discharger were charged with a permit violation for failing to perform its BMPs.

BMPs for the pharmaceutical manufacturing industry, which might include spill prevention, control provisions, and other aspects to prevent the release of raw materials, solvents, and process chemicals to wastewaters, would control the release of constituents listed in sections 307(a) and 311(e) of the CWA, such as methylene chloride, toluene, chloroform, and chloromethane (methyl chloride).

Information currently available to the Agency indicates that the following are activities and problems that can occur at pharmaceutical manufacturing plants that may be controlled by BMPs.

- Spills of solvents.
- Operator error resulting in dropped batches.
- Spilled or mishandled product or intermediate from internal transport operations.
- Failure of storage tank level indicators resulting in overfilling and spillage.
- Lack of dikes or berms in chemical storage areas.
- Use of drum storage which can result in poor housekeeping practices.
- Reaction vessel "burps" which release product and intermediate materials to roof vents. Rain then picks the pollutants released by the "burps" which are then released to stormwater.
- Material losses during tank truck loading and unloading operations.
- Complicated piping systems that increase the probability of operator error.
- Presence and use of floor drains that are used to dispose of spills to the sewer instead of a more controlled cleanup.

The above activities and accidents tend to discharge slug loads to the sewer systems which can cause interference, pass-through, or endanger worker safety at an on-site treatment facility or POTW. EPA is evaluating whether control over the above situations is adequately provided by the proposed effluent limitations guidelines and standards and the General Pretreatment Regulations, or if Best Management Practices specific to the Pharmaceutical Manufacturing Industry are warranted.

In 1986, the Domestic Sewage Study (DSS) found that categorical pretreatment standards were not always effective in handling accidental spills or irregular high strength batch discharges.

On July 24, 1990, the Agency promulgated amendments to the general pretreatment and NPDES regulations to enhance the control of toxic pollutant and hazardous waste discharges to POTWs (55 FR 30082). One of the amendments, 40 CFR 403.8(f)(2)(v), specifically addresses slug discharges. It provides that POTWs with approved pretreatment shall evaluate, at least once every two years, whether each significant industrial user (defined in 40 CFR 403.3(t)) needs a plan to control slug discharges. For the purposes of this provision, a slug discharge is any discharge of a non-routine, episodic nature, including but not limited to an accidental spill or a non-customary batch discharge. If a POTW decides that a slug control plan is needed, CFR 403.8(f)(2)(v) provides that the plan shall contain, at a minimum, the following elements:

- Description of discharge practices, including non-routine batch discharges;
- Description of stored chemicals;
- Procedures for immediately notifying the POTW of slug discharges, including any discharge that would violate a prohibition under 40 CFR 403.5(b), with procedures for follow-up written notification within five days;

- If necessary, procedures to prevent adverse impact from accidental spills, including inspection and maintenance of storage areas, handling and transfer of materials, loading and unloading operations, control of plant site run-off, worker training, building of containment structures or equipment, measures for containing toxic organic pollutants (including solvents), and/or measures and equipment for emergency response.

This provision sets forth only the minimal federal requirements for slug control plans. All POTWs (not just those required to establish federally approved pretreatment programs) may require such plans of any industrial user (not just significant industrial users) as necessary. Such plans could complement the provisions of BMPs.

2.0 POTENTIAL BMPs FOR THE PHARMACEUTICAL MANUFACTURING INDUSTRY

Preparation and implementation of BMP plans for the pharmaceutical manufacturing industry would primarily involve spill prevention and control. The BMP plan should contain the following key elements:

(1) Engineering analyses;
(2) Engineered controls and containment;
(3) Work practices;
(4) Preventive maintenance;
(5) Dedicated monitoring and alarm systems;
(6) Surveillance and repair programs; and
(7) Employee training.

The BMP plan should be prepared in accordance with good engineering practice. If the BMP plan calls for additional industry practices, facilities, equipment, procedures, or methods, not fully operational, the details of the installation and the operational start-up should be explained. The principal objective of the BMP plan should be to prevent losses and spills of process materials and solvents from equipment items in pharmaceutical manufacturing service; the secondary objectives should be to contain, collect, and recover at the immediate process area[1], or otherwise control, those spills and losses that do occur, and to minimize atmospheric emissions of volatile organic pollutants. The complete BMP plan should contain the elements described below.

[1]Immediate process area - The location at the facility where pharmaceutical chemical synthesis; fermentation; natural or biological extraction; mixing, compounding, and formulating; and pharmaceutical research facilities are located, generally the battery limits of the aforementioned processes. "Immediate process area" includes pharmaceutical manufacturing storage and spill control tanks located at the facility, whether or not they are located in the immediate process area.

2.1 Engineering Analyses

The BMP plan should be approved and signed by the facility manager. The plan should be based on a detailed engineering review of the pharmaceutical manufacturing operations, including but not limited to the following equipment and associated procedures: process equipment, storage tanks, pipelines and pumping systems, material transfer equipment, loading and unloading facilities, and other appurtenant equipment in pharmaceutical manufacturing service. The review should determine the magnitude and routing of potential leaks, spills and intentional releases during the following periods of operation:

- Process start-ups and shut downs;
- Response to off-specification batches;
- Maintenance;
- Storm events;
- Power failures; and
- Normal operations.

2.2 Engineered Controls and Containment

The BMP plan should also contain a detailed engineering review of existing pharmaceutical manufacturing containment facilities for the purpose of determining whether there is adequate capacity for collection and storage of anticipated intentional manufacturing diversions and sufficient contingency for collection and containment of spills, based upon good engineering practice. The review should consider whether adequate engineering control is provided on process and material handling area drains to prevent slug loads of process material from being intentionally or inadvertently released to the waste treatment or sewer system. The engineering review should also consider:

(1) The need for process wastewater diversion facilities to protect end-of-pipe wastewater treatment facilities from adverse effects of pharmaceutical manufacturing spills and diversions;

(2) The potential for contamination of storm water from the immediate process areas;

(3) The extent to which segregation and/or collection and treatment of contaminated storm water from the immediate process areas is appropriate; and

(4) The potential to reduce atmospheric emissions of volatile organic pollutants where engineered controls and containment are found to be inadequate by the detailed engineering review.

The BMP plan should specify specific required upgrades and improvements and provide a firm schedule for implementing such improvements and upgrades.

2.3 Work Practices, Preventive Maintenance, and Dedicated Monitoring and Alarm Systems

The BMP plan should specify the implementation of preventive maintenance practices, standard operating procedures, work practices, engineered controls and monitoring systems to prevent manufacturing losses and to divert pharmaceutical manufacturing process wastewaters (e.g. dropped batches) to containment facilities such that the diverted or spilled materials may be returned to the process or metered to the wastewater treatment system. Other standard operating procedures that should be considered include the use of tank level alarms, and associated preventive maintenance programs to ensure that alarms are functioning properly, to avoid overfilling tanks.

2.4 Surveillance and Repair

The BMP plan should include a program of regular visual inspections (at least once per operating shift) of equipment items in pharmaceutical manufacturing service and a program for repair of leaking equipment items. The repair program would encompass immediate repairs when possible and tagging for repair during the next maintenance outage those leaking equipment items that cannot be repaired during normal operations.

The owner or operator of the facility should also establish conditions under which production will be curtailed or halted to repair leaking equipment items or prevent manufacturing losses. The repair program should include tracking repairs over time to identify those equipment items where upgrade or replacement may be warranted based upon frequency and severity of leaks or failures. The owner or operator should maintain logs showing the date leaks were detected, the type of pharmaceutical manufacturing process, an estimate of the magnitude of the leak, the date of first attempt at repair, and the date of final repair. The logs should be maintained at the facility for review by the Regional Administrator or his designee during normal working hours.

2.5 Employee Training

An important aspect of the BMP would be a program of initial and refresher training of operators, maintenance personnel, and other technical and supervisory personnel who have responsibility for operating, maintaining, or supervising the operation and maintenance of equipment items and systems in pharmaceutical manufacturing service. At a minimum the training would cover the use of engineered controls and containment, work practices, preventive maintenance procedures, monitoring and alarm systems, and surveillance and repair aspects of the BMP. Refresher training should be conducted annually. The training would be documented and records of training would be maintained at the facility for review by the Regional Administrator or his designee during normal working hours.

The BMP plan should also specify a program of "boards of review" to evaluate each spill not contained at the immediate process area and any intentional diversion of pharmaceutical manufacturing material not contained in the immediate process area. The boards of review should be conducted as soon as practicable after the event and should be attended by the involved process operators, maintenance personnel, process engineering personnel, and supervisory personnel and environmental control staff. A brief report should be prepared for each board of review. The report should describe

the equipment items involved, the circumstances leading to the incident, the effectiveness of the corrective actions taken, and plans to develop changes to equipment and operating and maintenance practices to prevent recurrence. Reports of the boards of review should be included as part of the annual refresher training.

The BMP plan should also include a program to review any planned modifications to the pharmaceutical manufacturing facilities and any construction activities in the pharmaceutical manufacturing areas before these activities commence. The purpose of the reviews should be to ensure that pharmaceutical manufacturing spill prevention and control is considered as part of the planned modifications and that construction and supervisory personnel are aware of and can avoid possible manufacturing upsets, including spills, during manufacturing modification or construction.

Appendix C

Variability Factors Associated with Proposed Limitations for the Pharmaceuticals Manufacturing Industry

Table C-1

Variability Factors Associated with BPT Limitations

Pollutant or Pollutant Property	Subcategories A and C		Subcategories B and D	
	1-day	30-day	1-day	30-day
BOD_5	3.31	1.37	5.07	1.55
COD	2.25	1.29	3.31	1.35
TSS	3.96	1.39	4.60	1.47
Cyanide	3.25	1.72*	--	--

* 4-day variability factor.

Table C-2

Variability Factors Associated with BAT Limitations

Pollutant or Pollutant Property	Subcategories A and C		Subcategories B and D	
	1-day	4-day	1-day	4-day
Acetone	3.65	1.57	3.65	1.57
Acetonitrile	3.98	1.69	3.98	1.69
Ammonia	1.89	1.26	--	--
n-Amyl Acetate	3.98	1.69	3.98	1.69
Amyl Alcohol	3.98	1.69	3.98	1.69
Aniline	3.98	1.69	3.98	1.69
Benzene	3.98	1.69	3.98	1.69
2-Butanone (MEK)	3.98	1.69	3.98	1.69
n-Butyl Acetate	3.98	1.69	3.98	1.69
n-Butyl Alcohol	3.98	1.69	3.98	1.69
tert-Butyl Alcohol	3.98	1.69	3.98	1.69
Chemical Oxygen Demand (COD)	2.25	1.29	3.31	1.35
Chlorobenzene	3.98	1.69	3.98	1.69
Chloroform	2.21	1.32	2.21	1.32
Chloromethane	3.98	1.69	3.98	1.69
Cyclohexane	3.98	1.69	3.98	1.69
Cyanide	3.25	1.72	--	--
o-Dichlorobenzene	3.98	1.69	3.98	1.69
1,2-Dichloroethane	6.83	2.37	6.83	2.37
Diethylamine	3.98	1.69	3.98	1.69
Diethyl Ether	3.98	1.69	3.98	1.69
Dimethylamine	3.98	1.69	3.98	1.69
N,N-Dimethylacetamide	3.98	1.69	3.98	1.69
N,N-Dimethylaniline	3.98	1.69	3.98	1.69
N,N-Dimethylformamide	3.98	1.69	3.98	1.69
Dimethyl Sulfoxide	3.98	1.69	3.98	1.69
1,4-Dioxane	3.98	1.69	3.98	1.69
Ethanol	2.47	1.34	2.47	1.34
Ethyl Acetate	3.98	1.69	3.98	1.69

Table C-2

(Continued)

Pollutant or Pollutant Property	Subcategories A and C		Subcategories B and D	
	1-day	4-day	1-day	4-day
Ethylene Glycol	3.98	1.69	3.98	1.69
Formaldehyde	4.31	1.82	4.31	1.82
Formamide	3.98	1.69	3.98	1.69
Furfural	3.98	1.69	3.98	1.69
n-Heptane	3.98	1.69	3.98	1.69
n-Hexane	3.98	1.69	3.98	1.69
Isobutyraldehyde	3.98	1.69	3.98	1.69
Isopropanol	3.98	1.69	3.98	1.69
Isopropyl Acetate	3.98	1.69	3.98	1.69
Isopropyl Ether	3.98	1.69	3.98	1.69
Methanol	6.66	2.34	6.66	2.34
Methylamine	3.98	1.69	3.98	1.69
Methyl Cellosolve	3.98	1.69	3.98	1.69
Methyl Formate	3.98	1.69	3.98	1.69
Methylene Chloride	15.92	4.01	15.92	4.01
MIBK	3.98	1.69	3.98	1.69
2-Methylpyridine	3.98	1.69	3.98	1.69
Petroleum Naphtha	3.98	1.69	3.98	1.69
Phenol	2.50	1.37	2.50	1.37
Polyethylene Glycol 600	3.98	1.69	3.98	1.69
n-Propanol	3.98	1.69	3.98	1.69
Pyridine	3.98	1.69	3.98	1.69
Tetrahydrofuran	12.27	3.55	12.27	3.55
Toluene	3.98	1.69	3.98	1.69
Trichlorofluoromethane	2.73	1.47	2.73	1.47
Triethylamine	3.98	1.69	3.98	1.69
Xylenes	3.98	1.69	3.98	1.69

Table C-3

Variability Factors Associated with NSPS

Pollutant or Pollutant Property	Subcategories A and C		Subcategories B and D	
	1-day	4-day	1-day	4-day
Acetone	3.65	1.57	3.65	1.57
Acetonitrile	3.98	1.69	3.98	1.69
Ammonia	1.89	1.26	--	--
n-Amyl Acetate	3.98	1.69	3.98	1.69
Amyl Alcohol	3.98	1.69	3.98	1.69
Aniline	3.98	1.69	3.98	1.69
Benzene	3.98	1.69	3.98	1.69
2-Butanone (MEK)	3.98	1.69	3.98	1.69
n-Butyl Acetate	3.98	1.69	3.98	1.69
n-Butyl Alcohol	3.98	1.69	3.98	1.69
tert-Butyl Alcohol	3.98	1.69	3.98	1.69
Chlorobenzene	3.98	1.69	3.98	1.69
Chloroform	2.21	1.32	2.21	1.32
Chloromethane	3.98	1.69	3.98	1.69
Cyclohexane	3.98	1.69	3.98	1.69
Cyanide	3.25	1.72	--	--
o-Dichlorobenzene	3.98	1.69	3.98	1.69
1,2-Dichloroethane	6.83	2.37	6.83	2.37
Diethylamine	3.98	1.69	3.98	1.69
Diethyl Ether	3.98	1.69	3.98	1.69
Dimethylamine	3.98	1.69	3.98	1.69
N,N-Dimethylacetamide	3.98	1.69	3.98	1.69
N,N-Dimethylaniline	3.98	1.69	3.98	1.69
N,N-Dimethylformamide	3.98	1.69	3.98	1.69
Dimethyl Sulfoxide	3.98	1.69	3.98	1.69
1,4-Dioxane	3.98	1.69	3.98	1.69
Ethanol	2.47	1.34	2.47	1.34
Ethyl Acetate	3.98	1.69	3.98	1.69
Ethylene Glycol	3.98	1.69	3.98	1.69
Formaldehyde	4.31	1.82	4.31	1.82
Formamide	3.98	1.69	3.98	1.69

Table C-3

(Continued)

Pollutant or Pollutant Property	Subcategories A and C		Subcategories B and D	
	1-day	4-day	1-day	4-day
Furfural	3.98	1.69	3.98	1.69
n-Heptane	3.98	1.69	3.98	1.69
n-Hexane	3.98	1.69	3.98	1.69
Isobutyraldehyde	3.98	1.69	3.98	1.69
Isopropanol	3.98	1.69	3.98	1.69
Isopropyl Acetate	3.98	1.69	3.98	1.69
Isopropyl Ether	3.98	1.69	3.98	1.69
Methanol	6.66	2.34	6.66	2.34
Methylamine	3.98	1.69	3.98	1.69
Methyl Cellosolve	3.98	1.69	3.98	1.69
Methyl Formate	3.98	1.69	3.98	1.69
Methylene Chloride	15.92	4.01	15.92	4.01
MIBK	3.98	1.69	3.98	1.69
2-Methylpyridine	3.98	1.69	3.98	1.69
Petroleum Naphtha	3.98	1.69	3.98	1.69
Phenol	2.50	1.37	2.50	1.37
Polyethylene Glycol 600	3.98	1.69	3.98	1.69
n-Propanol	3.98	1.69	3.98	1.69
Pyridine	3.98	1.69	3.98	1.69
Tetrahydrofuran	12.27	3.55	12.27	3.55
Toluene	3.98	1.69	3.98	1.69
Trichlorofluoromethane	2.73	1.47	2.73	1.47
Triethylamine	3.98	1.69	3.98	1.69
Xylenes	3.98	1.69	3.98	1.69
BOD_5	3.08	1.43	5.32	1.58
COD	1.88	1.29	3.50	1.39
TSS	2.87	1.42	5.06	1.52

Table C-4

Variability Factors Associated with PSES

Pollutant or Pollutant Property	Subcategories A and C		Subcategories B and D	
	1-day	4-day	1-day	4-day
Acetone	10.45	3.23	10.45	3.23
Ammonia	1.31	1.10	--	--
n-Amyl Acetate	7.95	2.68	7.95	2.68
Amyl Alcohol	7.95	2.68	7.95	2.68
Aniline	7.95	2.68	7.95	2.68
Benzene	7.95	2.68	7.95	2.68
2-Butanone (MEK)	11.87	3.54	11.87	3.54
n-Butyl Acetate	7.95	2.68	7.95	2.68
n-Butyl Alcohol	7.95	2.68	7.95	2.68
tert-Butyl Alcohol	7.95	2.68	7.95	2.68
Chlorobenzene	7.95	2.68	7.95	2.68
Chloroform	7.95	2.68	7.95	2.68
Chloromethane	7.95	2.68	7.95	2.68
Cyclohexane	7.95	2.68	7.95	2.68
Cyanide	3.25	1.72	--	--
o-Dichlorobenzene	7.95	2.68	7.95	2.68
1,2-Dichloroethane	7.95	2.68	7.95	2.68
Diethylamine	7.95	2.68	7.95	2.68
Diethyl Ether	7.95	2.68	7.95	2.68
Dimethylamine	7.95	2.68	7.95	2.68
N,N-Dimethylaniline	7.95	2.68	7.95	2.68
1,4-Dioxane	7.95	2.68	7.95	2.68
Ethanol	6.27	2.23	6.27	2.23
Ethyl Acetate	7.95	2.68	7.95	2.68
Formamide	7.95	2.68	7.95	2.68
Furfural	7.95	2.68	7.95	2.68
n-Heptane	7.95	2.68	7.95	2.68
n-Hexane	7.95	2.68	7.95	2.68
Isobutyraldehyde	7.95	2.68	7.95	2.68

Table C-4

(Continued)

Pollutant or Pollutant Property	Subcategories A and C		Subcategories B and D	
	1-day	4-day	1-day	4-day
Isopropanol	7.82	2.60	7.82	2.60
Isopropyl Acetate	7.95	2.68	7.95	2.68
Isopropyl Ether	7.95	2.68	7.95	2.68
Methanol	8.48	2.76	8.48	2.76
Methylamine	7.95	2.68	7.95	2.68
Methyl Cellosolve	7.95	2.68	7.95	2.68
Methyl Formate	7.95	2.68	7.95	2.68
Methylene Chloride	8.09	2.79	8.09	2.79
MIBK	7.95	2.68	7.95	2.68
2-Methylpyridine	7.95	2.68	7.95	2.68
Petroleum Naphtha	7.95	2.68	7.95	2.68
n-Propanol	7.95	2.68	7.95	2.68
Pyridine	7.95	2.68	7.95	2.68
Tetrahydrofuran	5.97	2.18	5.97	2.18
Toluene	1.98	1.48	1.98	1.48
Trichlorofluoromethane	7.95	2.68	7.95	2.68
Triethylamine	7.95	2.68	7.95	2.68
Xylenes	7.95	2.68	7.95	2.68

Table C-5

Variability Factors Associated with PSNS

Pollutant or Pollutant Property	Subcategories A and C		Subcategories B and D	
	1-day	4-day	1-day	4-day
Acetone	3.07	1.54	3.07	1.54
Ammonia	1.31	1.10	--	--
n-Amyl Acetate	5.72	2.12	5.72	2.12
Amyl Alcohol	5.72	2.12	5.72	2.12
Aniline	5.72	2.12	5.72	2.12
Benzene	5.72	2.12	5.72	2.12
2-Butanone (MEK)	6.24	2.24	6.24	2.24
n-Butyl Acetate	5.72	2.12	5.72	2.12
n-Butyl Alcohol	5.72	2.12	5.72	2.12
tert-Butyl Alcohol	5.72	2.12	5.72	2.12
Chlorobenzene	5.72	2.12	5.72	2.12
Chloroform	5.72	2.12	5.72	2.12
Chloromethane	5.72	2.12	5.72	2.12
Cyclohexane	5.72	2.12	5.72	2.12
Cyanide	3.25	1.72	--	--
o-Dichlorobenzene	5.72	2.12	5.72	2.12
1,2-Dichloroethane	5.72	2.12	5.72	2.12
Diethylamine	5.72	2.12	5.72	2.12
Diethyl Ether	5.72	2.12	5.72	2.12
Dimethylamine	5.72	2.12	5.72	2.12
N,N-Dimethylaniline	5.72	2.12	5.72	2.12
1,4-Dioxane	5.72	2.12	5.72	2.12
Ethanol	5.72	2.12	5.72	2.12
Ethyl Acetate	5.72	2.12	5.72	2.12
Formamide	5.72	2.12	5.72	2.12
Furfural	5.72	2.12	5.72	2.12
n-Heptane	5.72	2.12	5.72	2.12
n-Hexane	5.72	2.12	5.72	2.12
Isobutyraldehyde	5.72	2.12	5.72	2.12

Table C-5

(Continued)

Pollutant or Pollutant Property	Subcategories A and C		Subcategories B and D	
	1-day	4-day	1-day	4-day
Isopropanol	5.72	2.12	5.72	2.12
Isopropyl Acetate	5.72	2.12	5.72	2.12
Isopropyl Ether	5.72	2.12	5.72	2.12
Methanol	5.48	2.06	5.48	2.06
Methylamine	5.72	2.12	5.72	2.12
Methyl Cellosolve	5.72	2.12	5.72	2.12
Methyl Formate	5.72	2.12	5.72	2.12
Methylene Chloride	8.09	2.79	8.09	2.79
MIBK	5.72	2.12	5.72	2.12
2-Methylpyridine	5.72	2.12	5.72	2.12
Petroleum Naphtha	5.72	2.12	5.72	2.12
n-Propanol	5.72	2.12	5.72	2.12
Pyridine	5.72	2.12	5.72	2.12
Tetrahydrofuran	5.97	2.18	5.97	2.18
Toluene	1.84	1.35	1.84	1.35
Trichlorofluoromethane	5.72	2.12	5.72	2.12
Triethylamine	5.72	2.12	5.72	2.12
Xylenes	5.72	2.12	5.72	2.12