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Preliminary Data Summary for the Pharmaceutical Manufacturing Point Source Category

PRELIMINARY DATA SUMMARY
FOR THE
PHARMACEUTICAL MANUFACTURING
POINT SOURCE CATEGORY

Office of Water Regulations and Standards
Office of Water
United States Environmental Protection Agency
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PREFACE

This is one of a series of Preliminary Data Summaries prepared by the Office of Water Regulations and Standards of the U.S. Environmental Protection Agency. The Summaries contain engineering, economic and environmental data that pertain to whether the industrial facilities in various industries discharge pollutants in their wastewaters and whether the EPA should pursue regulations to control such discharges. The summaries were prepared in order to allow EPA to respond to the mandate of section 304(m) of the Clean Water Act, which requires the Agency to develop plans to regulate industrial categories that contribute to pollution of the Nation's surface waters.

The Summaries vary in terms of the amount and nature of the data presented. This variation reflects several factors, including the overall size of the category (number of dischargers), the amount of sampling and analytical work performed by EPA in developing the Summary, the amount of relevant secondary data that exists for the various categories, whether the industry had been the subject of previous studies (by EPA or other parties), and whether or not the Agency was already committed to a regulation for the industry. With respect to the last factor, the pattern is for categories that are already the subject of regulatory activity (e.g., Pesticides, Pulp and Paper) to have relatively short Summaries. This is because the Summaries are intended primarily to assist EPA management in designating industry categories for rulemaking. Summaries for categories already subject to rulemaking were developed for comparison purposes and contain only the minimal amount of data needed to provide some perspective on the relative magnitude of the pollution problems created across the categories.

ACKNOWLEDGEMENTS

Preparation of this Preliminary Data Summary was directed by Dr. Frank H. Hund, Project Officer, of the Industrial Technology Division. Preparation of the economic analysis sections was directed by Mr. Rob Esworthy, Mr. Mitchell Dubensky, and Ms. Debra Nicoll of the Analysis and Evaluation Division. Mr. Rod Frederick of the Assessment and Watershed Protection Division was responsible for preparation of the environmental assessment analysis. Support was provided under EPA Contract Nos. 68-03-3412, 68-03-6302, 68-03-3366 and 68-03-3339.

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SUMMARY

The Industrial Technology Division (ITD) of the U.S. Environmental Protection Agency (EPA) conducted a study of the pharmaceutical manufacturing industry as a result of findings from the Domestic Sewage Study (DSS) and from concern for the potential discharge of toxic and hazardous pollutants from this industry. The purposes of the study were to

- provide technical, economic, and environmental bases to determine whether additional effluent limitation guidelines and standards to control the discharge of toxic and hazardous pollutants are necessary for the pharmaceutical manufacturing industry; and
- serve as a source of information to be used by permit writers and publicly owned treatment works (POTWs) in controlling hazardous wastes until final rules are published.

The study consisted of the following three interrelated but independent undertakings

- a technical support study;
- an economic impact analysis; and
- an environmental impact analysis.

The technical support study consisted of two parts: the collection and analysis of wastewater and waste solids samples from the pharmaceutical manufacturing industry, and the collection of sufficient information about the industry to develop a preliminary updated industry technical profile. The economic impact study consisted of a review and update of the economic profile of the industry and an analysis of the projected economic impact of additional wastewater regulation on the industry. The environmental impact study was an evaluation of the impacts of wastewater discharges from direct discharging pharmaceutical manufacturing facilities on their receiving streams and from indirect discharging facilities on publicly owned treatment works (POTWs) and their receiving streams.

Technical Support Study

For the technical study, EPA directed its efforts toward reviewing available information, as well as gathering new information through a sampling and analysis program, on the wastewater discharge of conventional, priority, and nonconventional pollutants from pharmaceutical manufacturing facilities. The sampling program, conducted at four pharmaceutical plants, helped characterize the industry's wastewater with respect to approximately 250 additional

compounds not included in previous sampling efforts. the sampling and in include in previous sampling efforts. The 250 compounds plus those included in previous sampling efforts constitute the ITD List of Analytes. This was the first ITD study to involve the sampling and analysis of sludges generated at wastewater treatment facilities in this industry.As part of the study, EPA estimated the total mass of conventional, priority, and nonconventional pollutants present in the wastewater generated by the pharmaceutical manufacturing industry. The following table summarizes EPA's bestestimate of the mass discharge of these pollutants, by direct and indirect discharging plants.

The results confirm the DSS findings that the pharmaceutical manufacturing industry discharges significant quantities of potentially hazardous compounds (especially priority and nonconventional volatile organic compounds [VOCs]) in raw wastewater. Based on information obtained in the screening and verification sampling program, EPA estimates that 4.7 million pounds per year of priority pollutant VOCs are discharged in the industry's raw wastewater. Based on information obtained in the recent sampling program EPA estimates that 16 million pounds per year of nonconventional pollutant VOCs are discharged in the industry's raw wastewater. Not shown on the table are 41 million additional pounds of VOCs not on the ITD List of Analytes which are estimated to be discharged annually in the industry wastewater. The industry's use, disposition, and the treatability of these additional compounds were not characterized in this report since they were not analyzed for in the past or in recent sampling programs.

Additional studies are warranted to accomplish the following:

- o verify EPA's present assessment of the discharge of priority pollutant VOCs;
- o better characterize the industry's discharge of nonconventional VOCs detected in the recent sampling program (wastewater sampling data are presently available for only six of the 464 plants in the industry);
- o expand the list of VOCs to be characterized in the wastewater discharges to include those commonly used by the industry (e.g., alcohols) which have never been listed for analysis in industry studies; and
- o obtain additional information on VOC control and treatment technologies (e.g., steam-stripping).

Economic Impact Analysis

The economic study consisted of a preliminary economic impact analysis of possible regulations affecting pharmaceutical

manufacturing facilities, particularly regulations limiting the release of volatile organic chemicals (VOCs). A profile of the industry, covering characteristics and trends for product groups, individual plants and companies, and the industry as a whole was included. In addition, this report presents an assessment of the ability of this industry to incur wastewater treatment costs.

The analysis described in this report was based on data currently available from secondary sources, data provided by earlier surveys of this industry, and data provided in the technical section of this document. The analysis was limited by the small amount of plant-specific data available and the age of some of this data. However, the main conclusions are well supported.

Three sections of this report present an economic profile of the pharmaceutical industry. Section VI describes the characteristics of the industry, including foreign trade, and its future outlook. Section VII provides a detailed description of the various product groups and their growth prospects. Section IX presents the characteristics of pharmaceutical plants, including their location, sales and employment levels.

Sections VIII, X, and XI present the economic impact analysis. Section VIII describes the financial characteristics of pharmaceutical companies based on a financial ratio analysis of 43 firms. Section X describes the procedures used to estimate compliance costs for each individual plant with wastewater discharge. Section XI presents the economic impacts on individual plants.

The economic analysis concludes that the pharmaceutical industry continues to be financially healthy and that most plants would experience little or no impact from regulating VOCs. However, some plants may experience substantial impacts from this level of compliance costs. For example, approximately 20 percent of the plants would experience a decline in profits of 10 percent or move.

Environmental Impact Analysis

The environmental impact study is presented in Section XII. The study evaluated the impacts of direct discharging pharmaceutical manufacturing plants on their receiving streams and the impacts of indirect discharging plants on the publicly owned treatment works (POTWs) to which the plants discharge and on the POTWs' receiving streams. Two different approaches were used in the analyses. The first approach involved projecting instream pollutant concentrations of volatile organic compound (VOCs) from industry-wide average pollutant concentrations. The projected pollutant concentrations were then compared to EPA water quality criteria or toxic effect levels.

The second approach employed actual VOC monitoring data from streams receiving direct wastewater discharges from pharmaceutical plants and monitoring data from streams receiving indirect discharges (via POTWs). Monitoring data were compared to EPA water quality criteria or toxic effect levels.

Water quality impacts were projected for 22 direct and 28 indirect discharging plants in subcategories A, B, and C. Fifteen VOCs were evaluated for direct dischargers, eight of which (all known or suspected carcinogens) were projected to exceed human health criteria in 86 percent of the stream segments. None of the VOCs evaluated were projected to exceed aquatic life criteria or toxic effect levels.

The effects of 28 indirect discharging plants were also evaluated. Twenty-one volatile pollutants were evaluated and six (all known or suspected carcinogens) were projected to exceed human health criteria for carcinogens in 60 percent of the streams receiving discharges from the POTWs to which the plants discharge. No volatile pollutants were projected to exceed aquatic life criteria or toxic effect levels. No inhibition of POTW treatment processes were projected for the 12 VOCs which have inhibition values. Sludge contamination could not be evaluated.

The impacts by VOCs, as monitored on five streams receiving direct discharges from pharmaceutical plants and on six streams receiving discharges from facilities discharging to POTWs were evaluated. Nine of the 15 pollutants evaluated were detected in four streams receiving direct discharges. Two of the pollutants exceeded human health criteria in three of the streams. Eight of the 21 pollutants evaluated were detected in four streams receiving indirect discharges. Three of the pollutants exceeded human health criteria in three of the streams. All of the pollutants are known or suspected carcinogens. None of the volatile pollutants exceeded aquatic life criteria or aquatic life toxic effect levels.

Volatile pollutant data for pharmaceutical facilities with monitoring requirements or limitations were also summarized. Eleven of the evaluated pollutants were monitored or limited for 36 percent of the direct discharging facilities. Eight of the evaluated pollutants were monitored or limited for 19 percent of the POTWs receiving discharges from indirect facilities.

ESTIMATED ANNUAL MASS LOADINGS
PHARMACEUTICAL MANUFACTURING INDUSTRY

Pollutants	Mass Loadings for Direct Dischargers (1,000 lb/yr)				Mass Loadings For Indirect Discharges (1,000 lb/yr)			
	Subcategories A, B, & C*		Subcategory D		Subcategories A, B, & C		Subcategory D	
	Raw Wastewater	Final Effluent	Raw Wastewater	Final Effluent	Raw Wastewater	Discharge to POTW	Raw Wastewater	Discharge to POTW
Conventional Pollutants								
o BOD5	83,000	5,900	4,100	300	169,000	169,000	5,600	5,600
o TSS	45,000	4,600	1,200	290	64,500	64,500	3,000	3,000
Priority Pollutants								
o Volatile Organics	2,000	77	240	6	2,400	2,000	18	18
o Semivolatile Organics	120	2	17	0.2	390	330	16	16
o Pesticides	--	--	--	--	0.02	0.02	--	--
o Metals	60	22	1.2	0.7	51	45	2	2
o Cyanide	22	7	0.3	0.2	4.3	4.1	0.3	0.3
Nonconventional Pollutants								
o COD	192,000	44,000	7,500	800	411,000	411,000	24,000	24,000
o Volatile Organics	5,100	**	1,000	**	7,700	**	2,200	**
o Semivolatile Organics	59	**	10	**	87	**	25	**
o Pesticides/Herbicides	63	**	11	**	92	**	26	**
Industry Characteristics								
o Number of Facilities	30*		21		130		155	
o Wastewater Flow (mgd)	21.38		3.54		31.1		8.8	

* Excluding Plant 12256
-- Negligible
** Insufficient data available

I. INTRODUCTION

This document comprises three interrelated but independent studies relating to wastewater discharges from the pharmaceutical manufacturing industry. The studies include a technical support study, an economic impact analysis, and an environmental impact analysis. The technical support section summarizes current information available on the wastewater discharge of conventional, priority, and nonconventional pollutants from pharmaceutical manufacturing facilities. As the result of recent sampling and other data-gathering efforts, it contains an updated technical industry profile and wastewater characterization. The recent sampling program helped characterize the industry's wastewater with respect to approximately 250 additional compounds not included in previous sampling efforts. The document also provides a technical basis for determining whether additional national regulations should be developed for the industry. Also included is information that can be used by permit writers and by waste treatment system operators in controlling hazardous wastes and hazardous constituents until final rules are published.

The pharmaceutical manufacturing point source category is defined and described in Section II, along with the subcategorization scheme used in previous rulemaking efforts. Section III characterizes pharmaceutical manufacturing wastewater in terms of the presence of conventional, priority, and nonconventional pollutants. Pollutant control and treatment technologies are discussed in Section IV.

The economic impact analysis consists of a review of economic data provided by earlier surveys of the pharmaceutical manufacturing industry and by some current data gathering efforts. The data were used to develop an updated economic profile of the industry. These data and data provided in the technical support section were the basis of an analysis of the impact that wastewater regulations of VOCs would have on the industry.

The analysis concludes that the pharmaceutical industry is financially healthy and that most plants would experience little or no impact from regulation of VOCs. However, the analysis does project that approximately 20 percent of the plants in the industry would experience a decline in profits of 10 percent or more.

Three sections of this report present an economic profile of the pharmaceutical industry. Section VI describes the economic characteristics of the industry, including foreign trade, and its future outlook. Section VII provides a detailed description of the various product groups and their growth prospects. Section IX presents the characteristics of pharmaceutical plants, including their location, sales and employment levels.

Sections VIII, X, and XI present an economic impact analysis. Section VIII describes the financial characteristics of pharmaceutical companies based on an analysis of financial ratios for 43 firms. Section X describes the procedures used to estimate compliance costs for each individual plant with wastewater discharge. Section XI presents the economic impacts on individual plants.

The environmental impact study evaluated the impacts of direct discharging pharmaceutical manufacturing plants on their receiving streams and the impacts of indirect discharging plants on the publicly owned treatment works (POTWs) to which the plants discharge and on the POTWs' receiving streams. A description of the study and the results are presented in Section XII.

The impacts of a number of VOCs on receiving streams from both direct and indirect dischargers were evaluated. Several known or suspected carcinogens were found to exceed or were projected to exceed human health criteria in one or more streams. However, none of the pollutants evaluated were found or projected to exceed aquatic life criteria or aquatic life toxic effect levels. No evaluated pollutants were projected to inhibit POTW treatment processes.

A. PURPOSE

The purposes of this decision document are to (1) establish technical, economic, and environmental bases for determining whether additional national regulations should be developed for the pharmaceutical manufacturing industry; and (2) provide information to guide permit writers and POTWs in controlling hazardous wastes and hazardous constituents until final rules are published.

B. AUTHORITY

1. Clean Water Act (CWA)

The U.S. Environmental Protection Agency (EPA) is required by Sections 301, 304, 306, and 307 of the Federal Water Pollution Control Act Amendments of 1972 and 1977 (the Clean Water Act, or CWA) to establish technology-based effluent limitations and standards to reduce the discharge of pollutants to the nation's waters. To achieve these goals, the Industrial Technology Division (ITD) is responsible for: (1) developing, proposing, and promulgating effluent limitations guidelines, new source performance standards, pretreatment standards, and Best Management Practices (BMPs) for industrial point source discharges; (2) assuring the adequacy and validity of scientific, economic, and technical data and findings used to support the effluent limitations and standards; (3) gathering, developing, and analyzing data and background information basic to the annual review and periodic revision of limitations and standards; and (4) developing technical information required for the judicial review of effluent limitations guidelines and standards.

This study was conducted under the authority of Sections 301(d) and 304(m) of the CWA, which require periodic review and revision of limitations promulgated pursuant to Sections 301, 304, and 306 of the CWA.

Section 301(d)

Any effluent limitation required by paragraph (2) of subsection (b) of this section shall be reviewed at least every five years and, if appropriate, revised pursuant to the procedure established under such paragraph.

Section 304(m)

Schedule for Review of Guidelines -

(1) Publication. Within 12 months after the date of the enactment of the Water Quality Act of 1987, and biennially thereafter, the Administrator shall publish in the Federal Register a plan which shall:

(A) establish a schedule for the annual review and revision of promulgated effluent guidelines, in accordance with subsection (b) of this section;

(B) identify categories of sources discharging toxic or nonconventional pollutants for which guidelines under subsection (b)(2) of this section and Section 306 have not previously been published; and

(C) establish a schedule for promulgation of effluent guidelines for categories identified in subparagraph (b), under which promulgation of such guidelines shall be no later than four years after such date of enactment for categories identified in the first published plan or three years after the publication of the plan for categories identified in later published plans.

(2) Public Review. The Administrator shall provide for public review and comment on the plan prior to final publication.

As part of its review of effluent limitations, EPA announced in a Federal Register Notice (50 FR 36638, September 9, 1985) that new information had been received concerning methylene chloride and other toxic volatile organic substances, including new data on air emissions of methylene chloride. The new information indicated that 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. EPA became concerned about air emissions of methylene chloride and other toxic volatile pollutants from biological treatment systems of pharmaceutical manufacturing

plants and POTWs receiving pharmaceutical wastewater. The presence of high concentrations of toxic and/or hazardous (i.e., those identified as hazardous constituents in the RCRA program) volatile organic compounds (VOCs) within sewer systems may endanger workers or create conditions leading to explosions and/or fires. Accordingly, EPA decided to review and update its data on the discharge of toxic and hazardous VOCs from pharmaceutical manufacturing facilities.

2. Resource Conservation and Recovery Act (RCRA)

In addition to responsibilities under the CWA, EPA is also charged by the 1976 RCRA with oversight of "cradle-to-grave" management of hazardous solid wastes. Section 3018(b) of RCRA is specifically related to this study.

> Section 3018(b): Revision of Regulations
>
> Within 18 months after submitting the report specified in subsection (a), the Administrator shall revise existing regulations and promulgate such additional regulations pursuant to this subtitle (or any other authority of the Administrator, including Section 307 of the Federal Water Pollution Control Act) as are necessary to assure that substances identified or listed under Section 3001 which pass through a sewer system to a publicly owned treatment works are adequately controlled to protect human health and the environment.

Section 3018(a) of RCRA, as amended by the 1984 Hazardous and Solid Waste Amendments (HSWA), directs EPA to submit a report to Congress concerning wastes discharged through sewer systems to POTWs that are exempt from RCRA regulation as a result of the Domestic Sewage Exclusion (DSE) of RCRA. The DSE, established by Congress in Section 1004(27) of RCRA, provides that solid or dissolved material in domestic sewage is not solid waste as defined in RCRA, and such materials cannot be considered a hazardous waste for RCRA purposes. The DSE applies to domestic sewage and industrial wastes discharged to POTW sewers that contain domestic sewage, even if the industrial wastes would otherwise be considered hazardous.

The report (the Domestic Sewage Study, or DSS) was prepared by EPA's Office of Water and submitted to Congress on February 7, 1986. The DSS examines the nature and sources of hazardous wastes discharged to POTWs, measures the effectiveness of EPA's programs in dealing with such discharges, and recommends ways to improve the programs to achieve better control of hazardous wastes entering POTWs.

Implicit in the DSE is the assumption that the pretreatment program mandated by the CWA can ensure adequate control of industrial discharges to sewers. This program, detailed under Section 307(b) of the CWA and implemented in 40 CFR Part 403, requires EPA to establish pretreatment standards for pollutants

discharged to POTWs by industrial facilities for those pollutants which interfere with, pass through, or are otherwise incompatible with the operation of POTWs.

In follow-up to the DSS, Section 3018(b) of RCRA directs the Administrator to revise existing regulations and promulgate any pretreatment standards controlling the discharge of individual hazardous constituents necessary to ensure that hazardous wastes discharged to POTWs are adequately controlled to protect human health and the environment. These regulations are to be promulgated pursuant to RCRA, Section 307 of the CWA, or any appropriate authority possessed by EPA. The regulations must be promulgated within 18 months after submission of the DSS to Congress (i.e., by August 1987).

The study concludes that the DSE should be retained at the present time, and recommends ways to improve various EPA programs under the CWA to obtain better control of hazardous wastes entering POTWs. In addition, the DSS recommends study efforts to fill information gaps, and indicates that other statutes (e.g., RCRA and the Clean Air Act) should be considered with the CWA to control either hazardous waste dischargers, receiving POTWs, or both, if the recommended research indicates the presence of problems not adequately addressed by the CWA.

A main recommendation of the study is that EPA review and amend categorical pretreatment standards to achieve better control of the constituents of hazardous wastes. The DSS recommends that EPA modify existing standards to improve control of organic priority and non-priority pollutants, and promulgate categorical standards for industrial categories not included in the Natural Resources Defense Council Consent Decree (NRDC v. Train, 8 ERC 2120, D.C.C., 1976).

Because the DSS findings identified pharmaceutical manufacturing facilities as a significant source of organic pollutants, and found that discharges from these facilities are largely unregulated for these pollutants, EPA decided to review and update its data on the discharge of hazardous nonconventional pollutants, as well as priority pollutants, from the industry.

While direct dischargers are not affected by the DSE, EPA has intentionally included direct dischargers in its review of hazardous waste discharges from pharmaceutical manufacturing facilities. EPA is interested in evaluating existing regulations established under the CWA for the control of both toxic priority pollutants and hazardous noncoventional pollutants at direct discharging facilities.

C. REGULATORY STATUS

Regulatory control of the discharge of priority and hazardous nonconventional pollutants from pharmaceutical manufacturing facilities involves both RCRA and the CWA. The following

paragraphs present an overview of the status of EPA's efforts to control hazardous waste discharges to POTWs with respect to RCRA, and to control the discharge of conventional, nonconventional, and priority pollutants to POTWs and the nation's waters with respect to the CWA.

1. Status of RCRA Regulations

On August 22, 1986, EPA published an Advance Notice of Proposed Rulemaking (ANPR), which was EPA's first step toward promulgating the regulations required by Section 3018(b) of RCRA (51 FR 30166). The ANPR contained no formal proposals for regulatory amendments. Instead, EPA suggested a range of preliminary approaches to improve the control of hazardous wastes discharges to POTWs and solicited comments. EPA has not yet determined whether to regulate the discharge of priority and hazardous nonconventional pollutants under the CWA or to copromulgate with RCRA.

2. Status of the CWA's Effluent Limitations Guidelines and Standards for the Pharmaceutical Manufacturing Point Source Category

EPA promulgated several effluent limitations guidelines and standards for the pharmaceutical manufacturing point source category under the authority of the CWA (40 CFR Part 439, Subparts A-E). These regulations were established for the following five subcategories of the industry

- Subpart A - Fermentation Products Subcategory
- Subpart B - Extraction Products Subcategory
- Subpart C - Chemical Synthesis Products Subcategory
- Subpart D - Mixing/Compounding and Formulation Subcategory
- Subpart E - Research Subcategory

The timing and status of regulations are discussed in the following paragraphs. A discussion of regulations that have been finalized is followed by a similar discussion on proposed regulations. Table I-1 a summarizes the timing and status of all CWA regulations.

a. Final Regulations. The following paragraphs summarize the limitations, new source performance standards, and pretreatment standards that have been finalized for the pharmaceutical manufacturing point source category.

Best Practical Control Technology (BPT) Limitations. BPT limitations are generally based on the average of the best existing performance by plants of various sizes, ages, and unit processes within the industry or subcategory for control of familiar (i.e., classical) pollutants. EPA promulgated interim

final BPT regulations for the pharmaceutical manufacturing point source category on November 17, 1976 (41 FR 50678).

The 1976 BPT regulations set monthly limitations for five-day biochemical oxygen demand (BOD5) and chemical oxygen demand (COD) based on percent removals for all subcategories. No daily maximum effluent limitations were established for these two parameters. The pH was set within the range of 6.0 to 9.0 standard units for all subcategories. The regulation also set maximum 30-day average total suspended solids (TSS) limitations for Subcategories B, D, and E only. No TSS limitations were established for Subcategories A and C. Subpart A (applicable to the fermentation operations subcategory) was amended on February 4, 1977, to improve the language referring to separable mycelia and solvent recovery (42 FR 6814). In addition, the amendment allowed the inclusion of spent beers (i.e., broths) in the calculation of raw waste loads for Subpart A in those instances where the spent beer is actually treated in the wastewater treatment system.

On October 27, 1983, EPA promulgated BPT limitations to (1) control the discharge of TSS from pharmaceutical plants in Subcategories A and C; (2) modify existing BPT BOD5, COD, and TSS effluent limitations in Subcategories B, D, and E; and (3) control the discharge of cyanide in Subcategories A, B, C, and D.

It is important to note that EPA excluded the research-only subcategory (Subcategory E) from development of further regulations beyond the 1983 BPT limitations. Pharmaceutical research does not fall within Standard Industrial Classification (SIC) Codes 2831, 2833, and 2834 (designated for study by EPA in the Settlement Agreement) and does not involve production and wastewater generation in appreciable quantities on a regular basis to warrant development of further national regulations.

Best Conventional Pollutant Control Technology (BCT) Limitations. The 1977 Amendments to the CWA added Section 301(b)(2)(E), which established BCT to control the discharge of conventional pollutants from existing industrial point sources. BCT limitations, like Best Available Technology Economically Achievable (BAT) limitations, represent the best existing performance in the industrial subcategory or category.

On December 16, 1986, EPA promulgated BCT limitations for existing pharmaceutical manufacturing facilities. Existing plants that use Subcategory A, B, C, and D operations to manufacture pharmaceutical products are covered by this regulation. Facilities that engage in pharmaceutical research (Subcategory E) only are not covered by this regulation. BCT limitations were set equal to BPT limitations promulgated on October 27, 1983 (48 FR 49808).

BAT Limitations. In general, BAT limitations represent the best existing performance in the industrial category or subcategory.

The CWA established BAT as the principal national means of controlling the direct discharge of toxic and nonconventional pollutants to U.S. waters. Final BAT limitations controlling the discharge of the toxic pollutant cyanide from pharmaceutical plants in Subcategories A, B, C, and D were promulgated on October 27, 1983.

New Source Performance Standards (NSPS). NSPS are based on the best available demonstrated technology because new plants have the opportunity to install the best and most efficient production processes and wastewater treatment technologies. On October 27, 1983, EPA promulgated NSPS limitations for pH and cyanide for Subcategories A, B, C, and D (48 FR 49810).

Pretreatment Standards for Existing and New Sources (PSES and PSNS). PSES and PSNS are designed to prevent the discharge of pollutants that pass through, interfere with, or otherwise are incompatible with the operation of POTWs. On October 27, 1983, EPA promulgated PSES and PSNS for only one priority pollutant (cyanide) for Subcategories A, B, C, and D (48 FR 49808).

b. Proposed Regulations. The following paragraphs summarize the limitations, new source performance standards, and pretreatment standards proposed for the pharmaceutical manufacturing point source category.

BAT Limitations. On November 26, 1982, EPA proposed BAT limitations designed to control the discharge of the nonconventional pollutant COD from pharmaceutical facilities.

Industry commented that the technical basis supporting the proposed COD limitations was inadequate and that EPA had not indicated which chemical pollutants it was attempting to control through the COD limitations. EPA decided to postpone a final decision on appropriate BAT limitations for COD until additional information was obtained regarding identity of pollutants that contribute to COD and applicable COD-removal technologies.

To respond to these additional information needs, EPA initiated a work/study program designed to

- determine the constituents of the high COD concentrations in biologically treated effluents of pharmaceutical manufacturing plants; and
- evaluate the ability of activated carbon adsorption (ACA) technologies to reduce the effluent COD levels.

An important part of the second objective involved demonstrating, through pilot plant studies, the capability of ACA technology to reduce pharmaceutical plant effluent COD levels. On April 27,

1984, ITD requested assistance from the Water Engineering Research Laboratory in Cincinnati, Ohio, in conducting the necessary pilot plant evaluations.

Two technologies were evaluated at a Subcategory A and C pharmaceutical manufacturing plant which used advanced biological treatment and reported high COD levels in its discharge monitoring report

- Powdered Activated Carbon (PAC) addition to the activated-sludge aeration basin for the treatment of raw wastewater
- Granular Activated Carbon (GAC) treatment of the secondary effluent

This study was conducted at a pharmaceutical plant from September 1 to December 7, 1984. However, operational problems occurred with the PAC pilot plant, causing the need for a follow-up study. The follow-up study was initiated in March 1987 and completed in July 1987. The final report on the study was made available.

In the preamble to the final regulations for the pharmaceutical manufacturing point source category (48 FR 49808), EPA stated that it had decided not to issue categorical regulations limiting methylene chloride, chloroform, benzene, and toluene discharges from pharmaceutical facilities. However, EPA received new information concerning possible harmful effects of discharges containing methylene chloride, and is reconsidering the question of whether to regulate methylene chloride and other VOC priority pollutants as well. As part of EPA's investigation, a notice was published in the Federal Register on September 9, 1985 (50 FR 36638) to (1) summarize previously available data; (2) make available new information; (3) present cost estimates associated with the ability of steam-stripping technology to reduce discharges of water-borne VOC priority pollutants; (4) request comments on the available information; and (5) seek additional information concerning steam-stripping technology.

NSPS. On October 27, 1983, EPA proposed NSPS for the conventional pollutants, BOD5 and TSS, for Subcategories A, B, C, and D (48 FR 49832). EPA has not promulgated NSPS for the nonconventional pollutant COD. Additional information regarding the identity of the pollutants that contribute to COD and applicable COD-removal technologies is required before EPA can evaluate COD control options. EPA is continuing its investigation of appropriate COD-removal technologies and their costs (refer to the previous discussion on BAT COD limitations).

As in the case of BAT, EPA decided not to issue NSPS limiting methylene chloride discharges from the pharmaceutical industry. However, if EPA reaches new conclusions on possible harmful effects of discharges containing methylene chloride and other

toxic VOCs, reconsideration of the decision not to issue regulations may be warranted.

PSES and PSNS. In the preamble to the final regulations for the pharmaceutical manufacturing point source category (48 FR 49808), EPA stated that it was not establishing pretreatment standards controlling the discharge of toxic pollutants, other than cyanide, from pharmaceutical plants. However, EPA received new information concerning possible harmful effects of discharges containing methylene chloride and other toxic pollutants, and is reconsidering the question of whether to regulate toxic pollutants discharged to POTWs.

TABLE I-1
CURRENT STATUS OF EFFLUENT LIMITATIONS GUIDELINES
AND STANDARDS FOR THE PHARMACEUTICAL
MANUFACTURING CATEGORY

	Subcategories A & C			Subcategories B & D			Subcategory E		
	Notices	Proposed Regulation	Final Regulation	Notices	Proposed Regulation	Final Regulation	Notices	Proposed Regulation	Final Regulation
BPT Limitations									
BOD5	--	--	11/17/76	--	--	11/17/76 10/27/83(a)	--	--	11/17/76 10/27/83(a)
TSS	--	--	10/27/83	--	--	11/17/76 10/27/83(a)	--	--	11/17/76 10/27/83(a)
pH	--	--	11/17/76	--	--	11/17/76	--	--	11/17/76
COD	--	--	11/17/76	--	--	11/17/76 10/27/83(a)	--	--	11/17/76 10/27/83(a)
Total Cyanide	--	--	10/27/83	--	--	10/27/83	--	--	--
BCT Limitations									
BOD5	--	--	12/16/86	--	--	12/16/86	--	--	--
TSS	--	--	12/16/86	--	--	12/16/86	--	--	--
pH	--	--	12/16/86	--	--	12/16/86	--	--	--
BAT Limitations									
COD	--	11/26/82	--	--	11/26/82	--	--	--	--
Total Cyanide	--	--	10/27/83	--	--	10/27/83	--	--	--
TTVO	9/9/85	--	--	9/9/85	--	--	--	--	--
NSPS									
BOD5	--	10/27/83	--	--	10/27/83	--	--	--	--
TSS	--	10/27/83	--	--	10/27/83	--	--	--	--
pH	--	--	10/27/83	--	--	10/27/83	--	--	--
COD	--	11/26/82	--	--	11/26/82	--	--	--	--
Total Cyanide	--	--	10/27/83	--	--	10/27/83	--	--	--
TTVO	9/9/85	--	--	9/9/85	--	--	--	--	--
PSES & PSNS									
Total Cyanide	--	--	10/27/83	--	--	10/27/83	--	--	--
TTVO	9/9/85	--	--	9/9/85	--	--	--	--	--

(a) Existing BPT, BOD5, TSS, and COD effluent limitations were modified for subcategories B, D, and E; refer to 48 FR 49808, October 27, 1983.

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TECHNICAL SUPPORT STUDY

II. DESCRIPTION OF THE INDUSTRY

This section presents information assembled to describe the pharmaceutical manufacturing industry. The data are derived from industry responses to EPA questionnaires, industry comments on proposed rulemakings, plant contacts, literature searches, and other sources. The industry profile was updated using information gathered in recent data collection efforts to provide the best current description of the industry. The manufacturing processes, the current subcategorization scheme, and the modes of wastewater discharge are discussed.

A. SUMMARY OF METHODOLOGY AND INFORMATION SOURCES

In this study, EPA directed its efforts toward reviewing available information, as well as gathering new information. The data-gathering efforts and subsequent information assessments conducted for this study can be divided into the following three tasks: gathering information to be used in the industry description (discussed in this section), obtaining analytical data used to characterize pharmaceutical manufacturing wastes (discussed in Section III), and information used to evaluate industry waste treatment systems (discussed in Section IV).

1. Review and Assessment of Existing Information

Previous regulatory efforts conducted by EPA provided substantial information regarding the industry profile, the manufacturing processes, and water use in the pharmaceutical manufacturing industry. The development documents, as well as the technical records supporting each of the rulemaking efforts, were initially reviewed to assess data gaps and requirements. This review identified the 308 Portfolio Survey as the major source of information pertaining to this study.

The 308 Portfolio Survey is an invaluable source of information for developing profiles and characterizing industry subcategories. It was the first major data source on the use and generation of priority pollutants by this industry.

The 308 Portfolio Survey was conducted in two phases. The original 308 Survey distributed questionnaires to members of the Pharmaceutical Manufacturers Association (PMA), in the fall of 1977. The second phase involved sending a second questionnaire to the remainder of the industry in the spring of 1979.

2. New Data

The major source of new data was a product patent search. Based on the initial review of available information, it was apparent that VOCs (being used as process solvents) were the likely priority and nonconventional pollutants of concern. In an attempt to better characterize VOC usage in the pharmaceutical industry, EPA reviewed all patents identified for the approximately 1,300 Subcategory A, B, and C products in its data base. This patent

review provided information regarding which VOCs were most likely to be used in the manufacture of pharmaceutical products, and which plants were most likely to be using them.

3. Industrial Profile and Subcategorization

Detailed information collected in previous data-gathering efforts was the basis for the industry profile. Information collected during the present study was compared to earlier information to update and revise (as necessary) the industry profile and subcategorization scheme.

B. INDUSTRY PROFILE

The pharmaceutical manufacturing industry encompasses the manufacture, extraction, processing, purification, and packaging of chemical materials to be used as medication for humans and animals.(1) The broad range of industry products includes natural substances extracted from plants or animals, chemically modified natural substances, synthetically made organic chemicals, metal-organics, and wholly inorganic materials. Packaging is equally varied. Some products are sold in bulk to other companies within the industry; some are sold to the public as creams, tablets, capsules, solutions, suspensions, and other forms.

EPA identified 464 facilities involved in the manufacture, extraction, processing, purification, or packaging of pharmaceuticals. The estimate is based primarily on the end result of two questionnaire mailings conducted by EPA under authority of Section 308 of the CWA.

The original 308 Questionnaire was developed by EPA with the cooperation of the PMA Environmental Task Force during the spring and summer of 1977. Questionnaires were sent only to PMA member firms and to nonmember plants included in previous EPA guidelines work. PMA member firms are the principal manufacturers of prescription pharmaceuticals, medical services, and diagnostics, and also produce a significant portion of over-the-counter drugs on the market. PMA members account for approximately 90 to 95 percent of U.S. sales of prescription products, and about 50 percent of the free world's total output of ethical pharmaceuticals. A total of 244 pharmaceutical manufacturing plants was identified from responses to the questionnaire.

A second 308 Questionnaire was developed during the fall of 1978 in an attempt to define the entire pharmaceutical population, obtain a more complete profile of the industry, and confirm the assumption that PMA member firms included in the initial survey do indeed represent the industry. This questionnaire identified 220 additional plants as pharmaceutical manufacturers.

However, since the mailing of the two questionnaires, four pharmaceutical plants (i.e., Plants 11111, 33333, 44444, and

55555) not in EPA's data base supplied data. EPA also learned that three facilities (i.e., Plants 20153, 12006, and 12112) are no longer manufacturing pharmaceuticals and that Plants 12084 and 20366 are really the same plant. Consequently, there are still 464 plants in EPA's data base.

Table II-1 shows the geographic distribution of the industry and the number of manufacturing plants by state and EPA region. Also shown are the average number of employees per plant and the average plant startup year. Most of the pharmaceutical plants are located in the eastern half of the U.S. (see Figure II-I). Of the 464 manufacturing plants in the comprehensive data base, almost 80 percent are in the East. New Jersey (with about 16 percent) and Region II (with approximately 36 percent) are the largest pharmaceutical manufacturing state and EPA region, respectively. The data show that Regions II, III, V, and VII (the Northeast and Midwest) generally have older plants than Regions IV, VI, VIII, and IX (the South and West). Puerto Rico, with close to 10 percent of the industry, has become a major pharmaceutical manufacturing center.

C. MANUFACTURING PROCESSES

Pharmaceuticals are manufactured by batch, continuous, and semi-continuous manufacturing operations. Batch-type production is by far the most common manufacturing technique, as can be seen by the production operation breakdown in Table II-2. The processes used in the manufacture of pharmaceuticals are (1) fermentation, (2) biological and natural extraction, (3) chemical synthesis, and (4) mixing/compounding/formulating. The four types of manufacturing operations are discussed in this section.

1. Fermentation

Fermentation is the usual method for producing most antibiotics and steroids. The fermentation process involves three basic steps: inoculum and seed preparation, fermentation, and product recovery. Production of a fermentation pharmaceutical begins 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 less critical fermentations, a single seed tank may serve several fermenters. In this type of operation, the seed tank is never emptied completely, so the remaining seed serves as the inoculum for the next batch. The seed tank is emptied, sterilized, and reinoculated only when contamination occurs.

TABLE II-1

PHARMACEUTICAL INDUSTRY
GEOGRAPHIC DISTRIBUTION

Location	Number of Plants	Percent of Total Plants	Average Number Employees Per Plant	Average Plant Startup Year(1)
EASTERN U.S. (REGIONS I-V)	367	79.1	268	1952
Connecticut	8	1.7	195	1963
Maine	0	0.0	-	-
Massachusetts	7	1.5	77	1961
New Hampshire	0	0.0	-	-
Rhode Island	1	0.2	(2)	(2)
Vermont	1	0.2	(2)	(2)
REGION I TOTALS	17	3.6	161	1960
New Jersey	75	16.1	346	1950
New York	43	9.2	211	1943
Puerto Rico	46	9.9	216	1970
Virgin Islands	2	0.4	13	-
REGION II TOTALS	166	35.7	239	1956
Delaware	2	0.4	121	1965
Maryland	6	1.3	65	1938
Pennsylvania	27	5.8	370	1949
Virginia	7	1.5	138	1950
West Virginia	2	0.4	151	-
District of Columbia	0	0.0	-	-
REGION III TOTALS	44	9.5	267	1950
Alabama	3	0.6	15	1958
Georgia	6	1.3	189	1956
Florida	8	1.7	95	1967
Mississippi	2	0.4	759	1949
North Carolina	12	2.6	456	1971
South Carolina	3	0.6	87	1968
Tennessee	10	2.2	301	1940
Kentucky	5	1.1	12	-
REGION IV TOTALS	49	10.5	250	1962

TABLE II-1 (continued)

PHARMACEUTICAL INDUSTRY
GEOGRAPHIC DISTRIBUTION

Location	Number of Plants	Percent of Total Plants	Average Number Employees Per Plant	Average Plant Startup Year(1)
Illinois	38	8.2	305	1951
Indiana	17	3.7	664	1944
Ohio	14	3.0	203	1929
Michigan	14	3.0	423	1933
Wisconsin	4	0.9	54	1957
Minnesota	4	0.9	41	-
REGION V TOTALS	91	19.6	351	1943
WESTERN U.S. (Regions VI-X) TOTAL	97	20.6	152	1962
Arkansas	2	0.4	1558	1970
Louisiana	2	0.4	9	-
Oklahoma	0	0.0	-	-
Texas	13	2.8	127	1967
New Mexico	0	0.0	-	-
REGION VI TOTALS	17	3.7	129	1968
Iowa	3	0.6	77	1963
Kansas	4	0.9	123	1954
Missouri	18	3.9	108	1943
Nebraska	4	0.9	201	1962
REGION VII TOTALS	29	6.2	117	1951
Colorado	5	1.1	96	1967
Utah	1	0.2	(2)	(2)
Wyoming	0	0.0	-	-
Montana	0	0.0	-	-
North Dakota	0	0.0	-	-
South Dakota	0	0.0	-	-
REGION VIII TOTALS	6	1.3	162	1968
Arizona	1	0.2	(2)	(2)
California	37	8.2	139	1967
Nevada	1	0.2	(2)	(2)
Hawaii	0	0.0	-	-
REGION IX TOTALS	39	8.6	137	1967

TABLE II-1 (continued)

PHARMACEUTICAL INDUSTRY
GEOGRAPHICAL DISTRIBUTION

Location	Number of Plants	Percent of Total Plants	Average Number Employees Per Plant	Average Plant Start-up Year(1)
Alaska	0	0.0	-	-
Idaho	0	0.0	-	-
Oregon	2	0.4	25	-
Washington	4	0.9	33	-
REGION X TOTALS	6	1.3	30	1955

(1) Since data concerning plant startup year were not solicited from the Supplemental 308 plants, the figures were calculated using only the original 308 plants responses.

(2) Employment and startup year figures are not presented to avoid disclosing individual plant data.

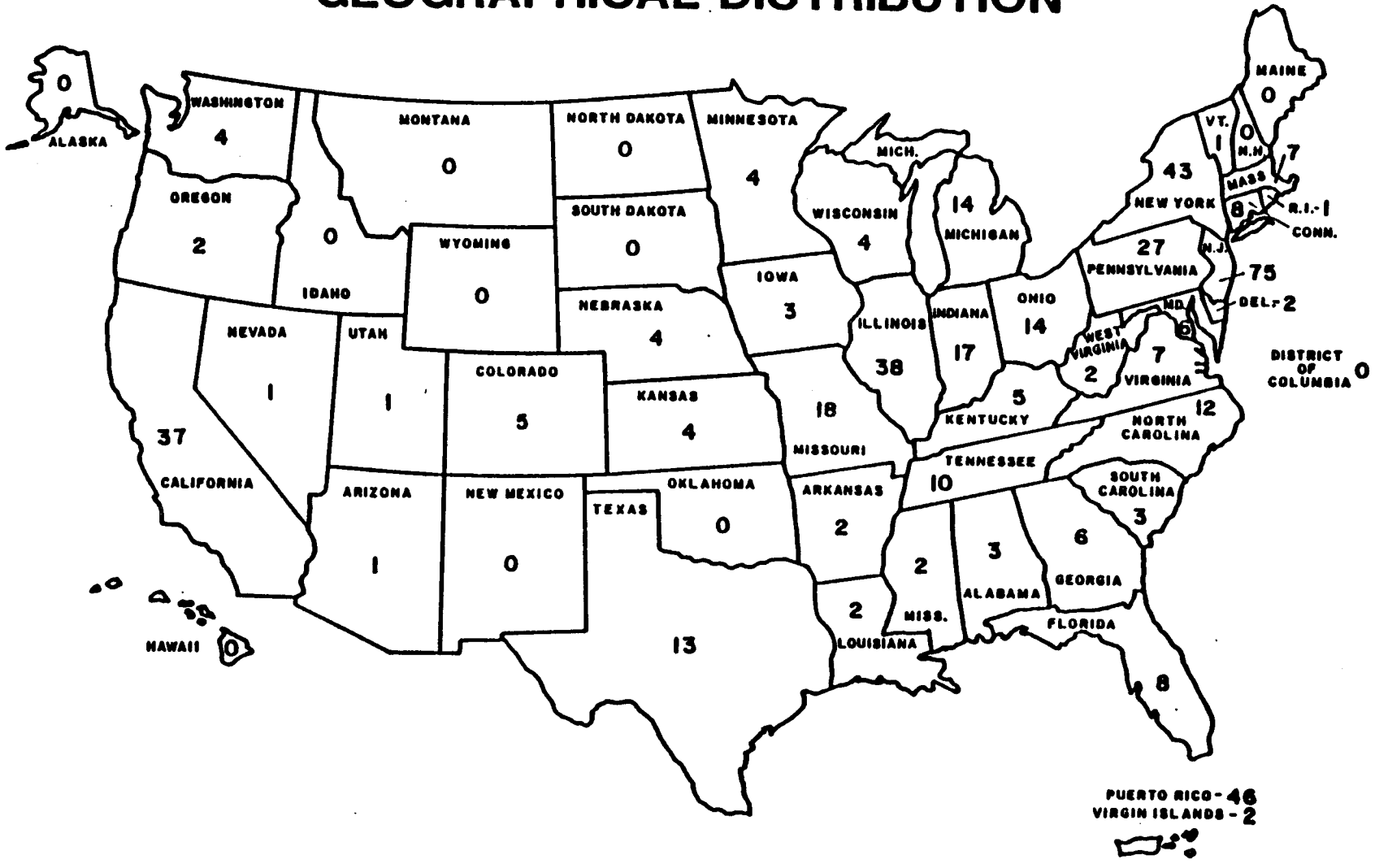
TABLE II-2

PRODUCTION OPERATION BREAKDOWN

Type of Operation	Number of Operations					
	Manufacturing Processes					
	Fermentation	Biological Extraction	Chemical Synthesis	Mixing/ Compounding/ Formulating	Total	Percent of Total Operation
Batch	32	76	129	359	596	87
Continuous	3	0	14	16	33	5
Semi-continuous	11	9	19	17	56	8
Total Number of Operations	46	85	162	392	685	100
Percent of Total Operations	7	12	24	57	100	
Percent of Subcategory Operations which are Batch	70	89	80	92	87	

NOTE: These data apply to 462 manufacturing plants. For two plants, no information was available on subcategories and types of production operations.

FIGURE II-1
PHARMACEUTICAL INDUSTRY
GEOGRAPHICAL DISTRIBUTION



Fermentation is conventionally a large-scale batch process. The cycle 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 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 of 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 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. The priority pollutant solvents most often used in fermentation operations are methylene chloride, benzene, chloroform, 1,1-dichloroethylene, and 1,2-trans-dichloroethylene.(1) Based on fermentation product patents, typical nonconventional solvents used in fermentation operations are acetone, ethyl acetate, and methanol (see Section III).

Direct precipitation using heavy metal precipitating agents is a 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 the priority pollutants known to be used in the precipitation process.(1)

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; it is then recovered by evaporation of the solvent.

Occasionally, a fermentation batch becomes infested with a phage; that is, a virus that attacks microorganisms. Phage infection is rare in a well-operated plant, but when it occurs, very large wastewater discharges may be necessary in a short period of time. Typically, the 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, to the extent that chemical disinfectants may be used, they can contribute to waste loads. An example of a commonly

used chemical disinfectant is phenol, a priority pollutant. Another fermentation wastewater source is the air pollution control equipment sometimes installed to clean fermentation waste off-gas. The air and gas vented from the fermenters usually contain odoriferous substances 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, light soluble organic compounds, and heavier insoluble organic oils and waxes. Wastewater from this source generally does not contain priority pollutants in appreciable concentrations.

The pollution contribution of spent beer results from the food materials contained in the beer, such as sugars, starches, protein, nitrogen, phosphate, and other nutrients. Fermentation wastes are very amenable to biological treatment. Although the spent beers, even in a highly concentrated form, can be satisfactorily handled by biological treatment systems, system upsets can be avoided if the wastes are first diluted to some degree with other wastewater. Dilution normally results from the equalization of fermentation wastes with other wastestreams. This prevents biota from receiving too high feed concentrations at one time.

Data from the 308 Survey generally show that wastewater from fermentation plants is characterized by high BOD, COD, and TSS concentrations; large flows; and a pH range of about 4.0 to 8.0.

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 stereosiomers, only one of which has pharmacological value. Extraction is an expensive manufacturing process. It requires collecting and processing large volumes of specialized plant or animal matter to produce small quantities of products.

The extraction process consists of a series of operating steps. In 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 was developed. 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 pots 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 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.

The nature of the pharmaceutical industry products dictates that any manufacturing facility maintain a standard of cleanliness higher than that required for most industrial operations. Because most of these plants are cleaned frequently, detergents and disinfectants are normally found in the wastewater.

As in the fermentation process, a small number of priority pollutants was identified as being used in the manufacturing of extractive pharmaceuticals.(2) The cations of lead and zinc are known to be used as precipitating agents. Phenol was identified as an equipment-sterilizing chemical, as well as an active ingredient. Otherwise, priority pollutants were found to be used only as processing solvents, including benzene, chloroform, and 1,2-dichloroethane. Based on Subcategory B product patent information, nonconventional pollutants that may be used as solvents are acetone, 1,4-dioxane, ethyl acetate, and methanol (see Section III).

Solvents are used in two ways in extraction operations. Firstly, they 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. Secondly, solvents are 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 achieve separation of 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; also, ammonia does 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 processes that generate (1) spent raw materials (e.g., waste plasma fractions, spent eggs, spent media broth, plant residues); (2) floor and equipment wash water; (3) chemical wastes (e.g., spent solvents); and (4) spills.

In general, the bulk of spent raw materials is collected and sent to an incinerator or landfill. Likewise, the nonrecoverable portions of the spent solvents are incinerated or landfilled. However, in both cases, portions of the residual materials find their way into a plant's wastewater. Floor and equipment washings and spills also contribute to ordinary waste loads.

Pollutant information for the biological/natural extraction operations in the pharmaceutical data base was limited due to the relatively small number of plants engaged in these operations. However, available data did allow for general conclusions to be drawn. Generally, wastewater from extraction plants is characterized by low BOD, COD, and TSS concentrations; small flows; and pH values of approximately 6.0 to 8.0.

3. Chemical Synthesis

Most compounds currently used as drugs are prepared by chemical synthesis (generally by a batch process). The basic major equipment item is the conventional batch reaction vessel, one of the most standardized equipment designs in industry.

Generally, the vessel is equipped with a motor-driven agitator and an internal baffle. 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. Vessels of this type are made in many different sizes, with capacities ranging from 0.02 to 11.0 m^2 or more.

The basic vessels may be fitted with many different attachments. Baffles usually contain sensors to measure the temperature of the reactor contents. An entire reactor may be mounted on load cells to accurately weight the reactor contents. Dip tubes are available to introduce reagents into the vessels below the liquid surface. 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. Agitators may be powered by two-speed motors or by variable-speed motor drives. Typically, batch reactors are installed with only the top heads extending above the plant operating floor to provide the operator with easy access for loading and cleaning. With other suitable accessories, the vessels can be used in several ways. Solutions can be mixed,

boiled, and chilled in them. By addition of reflux condensation, complete reflux operations (i.e., recycling of condensed vapors) are possible. By application of a vacuum, the vessels become evaporators. Solvent extraction operations can be conducted in them and, by operating the agitator at a slow speed, they serve as crystallizers.

Synthetic pharmaceutical manufacture consists of using one or more of these 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 to transfer the reactor contents into another similar vessel. At appropriate steps in the process, solutions are pumped either through filters or centrifuges, or into solvent recovery headers or waste sewers.

The vessels with an assembly of auxiliary equipment are usually arranged into independent process units; a large pharmaceutical plant may contain many such units. Each unit may be suitable for the complete or partial manufacture of many different pharmaceutical compounds. Only with the highest volume products is the equipment "dedicated" or modified to be suitable for only one process.

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, therefore, a process unit actively manufactures a specific compound. At the end of this campaign, another is scheduled to follow. The same equipment and operating personnel are then used to make a completely different product, using different raw materials, executing a different recipe, and creating different wastes.

The synthetic pharmaceuticals industry uses a wide variety of priority pollutants as reaction and purification solvents.(3) Water was reported to be used more often than would be expected in an industry whose products are organic chemicals. However, benzene and toluene were the most widely used organic solvents, because they are stable compounds that do not easily take part in chemical reactions. Similar, six-member ring compounds (e.g., xylene, cyclohexane, pyridine) also were reported as being used either in the manufacture of synthesized pharmaceuticals or resulting from unwanted side reactions.

A recent review of product patents for synthetic pharmaceuticals shows two additional priority pollutants used as solvents in chemical synthesis operations, chloroform and methylene chloride, and the nonconventional pollutants acetone, 1,4-dioxane,

ethylacetate, and methanol. Section III contains more detailed information on results of this review.

Solvents serve several functions in a chemical synthesis. They dissolve gaseous, solid, or viscous reactants to bring all reactants into close molecular proximity. They 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, and that would result in excessive temperature increases and unwanted side reactions.

There are other less obvious uses of solvents. One is the use of a solvent in the control of reaction temperature. It is common practice in a batch-type synthesis to select a solvent whose boiling point is the same as the desired reaction temperature and which is compatible with the reaction. 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. Such 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.

Essentially all production plants operate solvent recovery facilities that purify contaminated solvents for reuse. These facilities usually contain distillation columns, and may also include extraction facilities where still another solvent is used to separate impurities. Many wastes from the synthetic pharmaceutical industry will be discharged from these solvent recovery facilities. Aqueous wastes that may result from these operations include residues saturated with the recovered solvents. Another cause of solvent loss is storage practice. Bulk storage is usually in an unpressurized tank that is only partially filled. The level of the liquid in the tank rises and falls as liquid is added to or removed from the tank. The vapor in the tank above the surface of the liquid, therefore, is exhausted when the liquid level is rising. As the level falls, fresh air (or nitrogen from a padding system) is introduced. Even if no liquid is added or removed, the tank "breathes" as a result of temperature and barometric pressure changes. Each time a tank "exhales," the released vapor is saturated with solvent vapor. Rather large quantities of solvent can be lost to the atmosphere through this mechanism.

Chemical synthesis operations also produce large quantities of pollutants, normally measured as BOD and COD. Wastewater is generally produced with each chemical modification that requires the filling and emptying of the batch reactors. This wastewater can contain the unreacted raw materials, as well as some solvents. The effluent from chemical synthesis operations is the most complex to treat because of the many types of operations and chemical reactions (e.g., nitration, amination, halogenation, sulfonation, alkylation) which generate a large number of

different compounds.

These substances vary considerably with respect to toxicity and biodegradability. The production steps may generate acids, bases, cyanides, metals, and many other pollutants. In some instances, process solutions and vessel wash water may also contain residual solvents. Occasionally, this wastewater is incompatible with biological treatment systems. Although it is possible to acclimate the bacteria to the various substances, there may be instances where certain chemical wastes are too concentrated or too toxic to make this feasible. Thus, it may be necessary to equalize and/or chemically pretreat some process wastewater prior to conventional 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 spent water; and (5) spills. Wastewater from chemical synthesis plants can be characterized as having high BOD, COD, and TSS concentrations; large flows; and extremely variable pH, ranging from 1.0 to 11.0.

4. Mixing/Compounding/Formulating

Although pharmaceutically active ingredients are produced in bulk form, they must be prepared in dosage form for consumer use. Pharmaceutical compounds can be formulated into tablets, capsules, liquids, or ointments.

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. 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 drying. After the tablets have been coated and dried, they are bottled and packaged. 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 are in use. If wet scrubbers are used to capture solvent vapors from tablet-coating operations, the scrubbing water containing the solvents is likely to be sewered. If activated carbon is used to capture solvent vapors, the condensate from the steam used to regenerate the carbon is sometimes sewered.

Capsules are produced by first forming 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 the case of tablet production, some dust is generated. Although this is recycled, small amounts of waste dust must be disposed. Some glass and packaging waste from broken bottles and cartons also results from this operation.

Liquid preparations are formulated for injection or oral use. In both cases, the liquid 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 clean-up operations, spills, and breakage. Bad batches can create a solid waste disposal problem.

The primary objective of mixing/compounding/formulating operations is to convert the manufactured products into a final, dosage form. The necessary production steps have typically small wastewater flows because very few of the unit operations generate wastewater. The primary uses of water in the actual formulating process are for cooling water in the chilling units and for equipment and floor washing.

Wastewater sources from mixing/compounding/formulating operations are (1) floor and equipment wash water, (2) wet scrubbers, (3) spills, and (4) laboratory wastes. The use of water to clean out mixing tanks can flush materials of unusual quantity and concentration into the plant sewer system. The washouts from recipe kettles 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 data base shows that wastewater from mixing/compounding/formulating plants normally has low BOD, COD, and TSS concentrations; relatively small flows; and pH values of 6.0 to 8.0.

D. INDUSTRY SUBCATEGORIZATION

The pharmaceutical industry subcategories selected and established for data analysis are as follows:

Subcategory A - Fermentation
Subcategory B - Biological Extraction
Subcategory C - Chemical Synthesis
Subcategory D - Mixing/Compounding/Formulating

These are identical to four of the subcategories established in the original BPT rulemaking (41 FR 50676). An additional subcategory (Subcategory E - Research) was identified earlier in the 1976 Development Document. However, since research 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, it is not included in this study.

Table II-3 presents a distribution of the industry by manufacturing subcategory. Subcategory D (Mixing/Compounding/Formulating) is the most prevalent pharmaceutical manufacturing operation, with 80 percent of the plants in the industry engaged in this activity. Fifty-eight percent of these plants conduct Subcategory D operations only. The remainder also have operations in other subcategories.

1. Subcategory Characteristics

There are discernible differences among the subcategories when viewed in terms of effluent concentration averages or ranges and wastewater flow rates. These differences support the identification and use of these subcategories for regulatory purposes.

a. Subcategory A - Fermentation. Fermentation is the basic processing method used in the production of most antibiotics and steroids. The steps used are (1) preparation of a seed, (2) inoculation of the nutrient batch, (3) fermentation of the nutrient raw materials, and (4) recovery of the product by means such as extraction, precipitation, or ion exchange.

Fermentation processes are typically very large water users. Spent beers are the major source of characteristically high BOD5, COD, and suspended solids levels in the wastewater. Average raw waste flow, BOD5, COD, and TSS values for Subcategory A plants are 0.622 mgd, 1,668 mg/l, 3,452 mg/l, and 1,023 mg/l, respectively.(4)

b. Subcategory B - Biological Extraction. Biological or natural extraction is the extractive removal of therapeutic products from natural sources such as plant parts (e.g., roots and leaves), animal parts (e.g., glands), and parasitic fungi (e.g., molds). In contrast to fermentation, biological extraction processes are normally small-volume water users with lower BOD5, COD, and suspended solids levels. Average raw waste flow, BOD5, COD, and TSS values for Subcategory B plants are 0.197 mgd, 42 mg/l, 132 mg/l, and 93 mg/l, respectively.(4)

c. Subcategory C - Chemical Synthesis. Chemical synthesis is used widely in the manufacture of many drugs currently marketed. Most production is in batch reactors, which can be used for a wide variety of process steps (i.e., heating, cooling, mixing, evaporation, condensation, crystallization, and extraction).

TABLE II-3

SUBCATEGORY BREAKDOWN

Manufacturing Subcategory Combination	Number of Plants	Percent of Total Plants
A	3	0.6
AB	1	0.2
ABC	2	0.4
ABCD	8	1.7
ABD	4	0.9
AC	3	0.6
ACD	10	2.2
AD	6	1.3
B	21	4.5
BC	12	2.6
BCD	8	1.7
BD	23	5.0
C	50	10.8
CD	43	9.3
D	268	57.8
Not Available	2	0.4
Total Plants	464	100.0

The reactor vessels generally are constructed of glass-lined or stainless steel. Their versatility permits multiple functions and production of many different compounds.

Chemical synthesis processes are relatively large water users with high pollutant loadings. Also, a wide variety of chemical pollutants can be expected. Average raw waste flow, BOD5, COD, and TSS values for Subcategory C plants are 0.477 mgd, 2,385 mg/l, 4,243 mg/l, and 414 mg/l, respectively.(4)

d. Subcategory D - Mixing/Compounding/Formulating.
In formulation (i.e., mixing, compounding, and formulating), pharmaceuticals are prepared in such useable forms as tablets, capsules, liquids, and ointments. Active ingredients are physically mixed with filler, formed into dosage quantities, and packaged for distribution.

Formulation is normally a low-level water user (in many cases a dry operation) with low pollutant levels. Average raw waste flow, BOD5, COD, and TSS values for Subcategory D plants are 0.296 mgd, 339 mg/l, 846 mg/l, and 308 mg/l, respectively.(4)

Variations in process routes used by different producers are common in the pharmaceutical industry. Process variations (in chemical synthesis plants manufacturing the same product) occur because different starting materials and reaction sequences are used. Two plants making the same product, but using different starting materials, may use different reaction sequences. It is possible that once a common intermediate compound is derived, the remaining processing steps will mirror each other. Even if the same starting material is used by different plants, it is possible, due to the complexity of a synthesis, that several feasible routes to an end product exist. The decision as to which route will be used can depend on the chemical yield (i.e., economics), patent coverage, corporate history, or even personal preferences. In some cases, synthetic routes are modified to use less toxic and oxygen-demanding substances or to generate fewer of these substances as by-products.

In fermentation and material extraction processes, the major differences will occur in the extraction method. In many cases, extractions can be accomplished by any number of solvents. Choice of a solvent will depend on environmental impact, company history, economics, patents, and other factors. Due to the number of variables involved, it is not surprising that these processes vary widely between plants.

2. Subcategorization Analysis

As explained in the preamble to the regulation proposed in November 1982 (47 FR 53584; November 26, 1982), EPA proposed to combine four subcategories into a single subcategory. Along with comments on the November 1982 proposal, EPA received new plant data that were added to the existing data base. EPA statis-

tically analyzed these data on influent and effluent characteristics of all direct dischargers to determine if the proposed change to create a single subcategory was appropriate. A discussion of the data sources and the statistical comparisons used is presented in detail in Section IV of the 1983 Final Development Document.(4) Results of the statistical analysis are summarized in the following paragraph.

Analyses indicate that the subcategorization scheme should separate fermentation and chemical synthesis plants (Subcategory A and C plants) from extraction and formulation plants (Subcategory B and D plants), insofar as regulations controlling the discharge of conventional pollutants and the nonconventional pollutant COD are concerned. Specifically, the analyses show that the influent and effluent conventional pollutant concentrations and COD concentrations, as well as discharge flows of Subcategory A and C plants, are similar and that these same characteristics are also similar for Subcategory B and D plants. The analyses also indicate that characteristics of the Subcategory A and C plant group are not similar to the corresponding characteristics of the Subcategory B and D plant group. These differences indicate that different effluent discharge levels of conventional and nonconventional pollutants would be expected when plants in these groups used the same control technology. However, the existing subcategory scheme accommodates these differences. Because permitting authorities and the regulated industry are familiar with the original subcategorization scheme and the format in the Code of Federal Regulations, EPA decided to maintain the existing subcategorization scheme.

E. METHOD OF DISCHARGE

Table II-4 presents information on methods of wastewater discharge at the 464 pharmaceutical manufacturing plants in EPA's data base. At 11 percent of the plants, wastewater is treated on-site in a treatment system operated by plant personnel and is discharged directly to U.S. waters. At 62 percent of the pharmaceutical facilities, wastewater is discharged to a POTW. At 27 percent of the pharmaceutical plants, wastewater either is not generated or is not discharged to navigable waters or POTWs.

TABLE II-4

SUMMARY OF METHODS OF DISCHARGE
AT PHARMACEUTICAL PLANTS

Method of Discharge	No. of Plants	Wastewater (mgd)
Direct Dischargers	52	24.9*
Indirect Dischargers	285	39.9
Zero Dischargers	127	--
Total Plants	464	64.8*

* Wastewater flow estimate excludes flow from Plant 12256. It was not possible to determine representative flow for Plant 12256 from the available data.

III. WASTE CHARACTERIZATION

EPA, through several data-gathering efforts, studied wastewater of the pharmaceutical manufacturing industry. These efforts provided the baseline data necessary for determining the significant pollutants present in the wastewater of the industry and, subsequently, the regulatory scope for the pharmaceutical manufacturing point source category.

Past efforts focused on determining the presence and levels of conventional pollutants (i.e., BOD5, TSS, and pH), priority pollutants, and nonconventional pollutants (i.e., COD). The most recent efforts focused on determining the presence and levels of approximately 250 additional pollutants not previously analyzed for in this industry's wastes.

This section summarizes: (1) past data collection efforts conducted to characterize the industry's wastes with respect to conventional pollutants, priority pollutants, and nonconventional pollutants; (2) recent data collection efforts conducted to characterize industry waste with respect to approximately 250 additional nonconventional pollutants; and (3) an estimate of the annual mass discharge of conventional, priority, and noncoventional pollutants by the industry.

A. SUMMARY OF METHODOLOGY AND DATA SOURCES

In this study, EPA directed its efforts toward reviewing available information, as well as gathering new information through a sampling and analysis program, regarding the discharge of priority and hazardous nonconventional pollutants from pharmaceutical manufacturing facilities. The data-gathering efforts and subsequent information assessments conducted for this study were divided into the following tasks.

1. Review and Assessment of Existing Information

Previous regulatory efforts conducted by EPA provided substantial information regarding wastewater and other waste characteristics in the pharmaceutical manufacturing industry. The development documents, as well as the technical records supporting each of the rulemaking efforts, were initially reviewed to assess data gaps and requirements. This review identified the following major sources of information pertaining to this study (discussed in detail in Section B).

- 308 Portfolio Survey. A survey distributed in 1977 and 1979.
- PEDCo Reports. A literature review to identify priority pollutants associated with the production of various pharmaceutical products.
- OAQPS Study. A 1975 survey to determine the use and disposition of VOCs.

- Toxic Volatile Organics (TVO) Questionnaire. An EPA survey requesting analytical information on TVO levels in wastewater.

- State and Local Data. Limited state and local POTW data were obtained.

- RSKERL/ADA Study. "Industry Fate Study" to determine the fate of specific priority pollutants as they pass through a biological treatment system.

- Screening and Verification Sampling Program. An EPA Sampling Program for priority and traditional pollutants.

2. New Data Sources.

The following sources of new data are discussed in detail in Section C.

- OAQPS Data. A supplement to the 1975 study.

- Sampling and Analysis Program. A program to obtain wastewater and wastewater treatment plant sludge samples at four pharmaceutical manufacturing facilities. The samples were analyzed for conventional, priority, and nonconventional pollutants on the ITD List of Analytes.

3. Water Use, Solids Generation, and Waste Characterization

The data bases previously established by EPA and the new data were reviewed to update water use and waste characterization for the industry.

4. Pollutant Mass Load Estimates

The analytical data base was updated to include data obtained during previous industry studies and the current study. The data base was used to estimate the mass load of conventional, priority, and nonconventional pollutants discharged in the wastewater and waste solids generated by the industry.

B. EXISTING DATA SOURCES

Past data collection efforts conducted by EPA focused on determining the presence and levels of conventional pollutants (i.e., BOD5, TSS, and pH), priority pollutants, and nonconventional pollutants (i.e., COD). This section briefly discusses these past data collection efforts and summarizes the results.

1. Conventional and Nonconventional Pollutants

The CWA defined four conventional pollutants: BOD5, TSS, pH, and fecal coliform. An additional pollutant, oil and grease, was

defined by EPA as a conventional pollutant under procedures established in Section 304 of the CWA. As a result of past efforts, effluent limitations were established for control of the conventional pollutants BOD5, TSS, and pH in discharges from the pharmaceutical manufacturing industry.

The nonconventional pollutants of COD, total organic carbon (TOC), color, ammonia, nitrogen, and phosphorus were considered for regulation in past rulemaking efforts. Of these, only COD was chosen as a representative of a specific and persistent pollution problem across the industry.

These pollutants (i.e., BOD5, TSS, COD, and pH) were identified in all plant effluents analyzed. Pollutant levels in treatment plant influent and effluent streams were frequently high, particularly at Subcategory A and C facilities (fermentation and chemical synthesis, respectively).

Efforts to characterize the wastewater of this industry with respect to conventional and nonconventional pollutants are summarized in the following paragraphs.

a. 308 Survey. The pharmaceutical manufacturing industry was surveyed in 1978 to obtain wastewater data and related plant information. The first 308 Questionnaire was sent to PMA member companies. The questionnaire is included as Appendix B of the 1982 Proposed Development Document.(5) The second phase of this survey was aimed at the remainder of the industry; the questionnaire is in Appendix D of the Proposed Development Document. Substantial differences in both the form and content of these questionnaires resulted from shifts of program emphasis between the times of their distribution. Recipients are listed in Appendices C and E of the Proposed Development Document. Survey/ response statistics are reviewed in Section II of the Proposed Development Document. Traditional pollutant (i.e., BOD5, COD, and TSS) levels, as indicated in the 308 Portfolio data, and flow data are summarized in Appendices I and J of the Proposed Development Document, respectively.

b. Long-term Data. EPA selected 22 plants to provide long-term BOD5, COD, and TSS data on their end-of-pipe (EOP) treatment system's influents and effluents. The development of a long-term data base, covering at least a full year's data for representative plants, was necessary to allow EPA to establish performance averages for representative groups of industry treatment plants in terms of both pollutant levels and effluent variability. A summary of long-term data is presented in Table III-1.

TABLE III-1

SUMMARY OF LONG-TERM DATA
(Average Values for Daily Data)

Plant	Sub-category	Flow (mgd)	RAW WASTE LOAD						FINAL EFFLUENT					
			BOD5		COD		TSS		BOD5		COD		TSS	
			(mg/ℓ)	(lb/d)	(mg/ℓ)	(lb/d)	(mg/ℓ)	(lb/d)	(mg/ℓ)	(lb/d)	(mg/ℓ)	(lb/d)	(mg/ℓ)	(lb/d)
12015	D	0.101	232.6	192.8	552.7	462.5	123.8	102.6	9.7	7.8	44.0	35.4	10.8	8.7
12022	A C	1.448	2,141.6	25,880.0	.	.	.	.	110.2	1,308.3	.	.	84.9	991.0
12026	C	0.161	3,670.0	4,869.7	7,334.7	9,700.6	87.9	113.5	108.1	136.4	1,221.8	1,644.7	283.7	377.8
12036	A C	1.092	1,570.8	14,490.0	3,542.3	32,358.0	1,059.1	9,812.4	33.0	293.6	444.5	3,919.7	78.1	720.7
12097	C D	0.064	1,577.3	844.3	1,884.8	984.7	.	.	49.3	30.6	37.6	20.4	18.1	10.5
12098	D	0.006	.	.	.	.	.	.	409.9	12.8	.	.	392.1	16.2
12117	B	0.101	34.5	26.5	95.4	76.6	.	.	1.9	1.7	24.5	20.3	16.0	12.8
12123	C D	0.931	.	.	.	.	.	.	.	.	.	.	.	.
12160	D	0.029	490.2	78.0	2,160.4	449.6	1,615.2	282.2	166.9	41.8	516.7	137.5	115.4	20.3
12161	A C D	1.653	1,538.9	21,142.0	4,332.6	59,231.0	795.9	10,680.0	19.8	276.4	850.2	11,727.0	31.6	436.7
12186	C D	0.037	.	.	.	.	.	.	77.0	27.1	447.5	150.2	119.3	40.2
12187	C	1.065	.	.	.	.	.	.	707.3	6,380.9	.	.	60.5	538.1
12236	C	0.816	742.0	5,149.6	2,009.7	13,277.0	.	.	126.2	886.3	501.9	3,451.8	62.0	431.0
12248	D	0.110	294.4	281.3	473.9	455.2	.	.	26.0	25.5	95.9	90.9	60.4	59.1
12257	A B C D	0.755	2,961.7	18,750.0	.	.	1,009.4	6,306.4	228.4	1,439.5	.	.	715.3	4,403.8
12294	C D	0.118	1,584.3	1,537.6	3,429.6	3,332.3	.	.	44.7	43.9	232.3	228.9	59.2	60.5
12307	D	0.002	.	.	.	.	.	.	11.4	0.2	106.4	2.1	32.3	0.6
12317	D	0.740	1,003.7	5,985.6	1,102.3	6,887.7	41.4	247.7	7.9	43.7	42.3	254.8	9.8	59.5
12420	B D	0.164	.	.	.	.	.	.	786.8	1,097.2	.	.	966.4	1,328.7
12439	C D	.	.	.	.	.	.	.	495.4	.	971.2	.	.	.
12459	D	0.049	69.5	18.1	298.9	91.9	58.6	23.7	3.8	1.6	112.8	48.3	16.7	6.7
12462	A	0.209	1,805.0	3,074.8	5,168.2	8,866.5	2,012.9	3,308.7	726.8	1,272.6	2,499.3	4,247.0	2,020.4	3,391.8

Notes: Period (.) indicates no data reported.

c. 308 Supplemental Survey. Selected pharmaceutical plants were surveyed in 1984 to obtain treatment data on biological treatment and effluent filtration technologies. The data consist of individual observations of pollutants (e.g., BOD5, TSS, and COD) at specified points within each plant's treatment system. The period covered by the individual plant observations varies from four to 36 months. Summaries of the supplemental biological treatment data and the effluent filtration data are presented in Tables III-2 and III-3, respectively.

2. Priority Pollutants

The Settlement Agreement list of priority pollutants and classes of priority pollutants potentially includes thousands of specific compounds. However, for rulemaking purposes, EPA selected 126 specific pollutants for consideration; these are listed in Table III-4.

Because of the diversity of processes and materials used by the industry, virtually every priority pollutant compound listed in the modified comprehensive Settlement Agreement was found to be present in the effluent of at least one plant. However, cyanide was the only priority pollutant detected frequently and at sufficient levels to warrant development of national regulations in past rulemaking efforts.

a. 308 Portfolio Survey. The 308 Portfolio Survey was an invaluable source for developing profiles and characterizing industry wastes. It was the first major source of data on the use and/or generation of priority pollutants by this industry.

The 308 Portfolio Survey allowed quantification of the nature and extent of priority pollutants in the pharmaceutical manufacturing industry. Of the 464 plants in the 308 Portfolio Survey data base, 212 responded to the questions concerning priority pollutants. Of the 115 different priority pollutants identified, chloroform, methylene chloride, phenol, toluene, and zinc were reported as the most frequently used raw materials for manufacturing operations. None of the priority pollutants was reported by as many as 10 respondents as being intermediate or final products. Some priority pollutants (e.g., the pesticide-related compounds endrin and heptachlor) were reported as being analyzed in the effluents of the manufacturing plants (believed to be from non-pharmaceutical sources), but not as being a pharmaceutical manufacturing raw material or final product.

Although the industry uses and therefore might discharge a large number of priority pollutants, the 308 Portfolio Survey data base indicates that broad occurrence of specific chemical compounds is limited. Priority pollutant information submitted by pharmaceutical manufacturing plants is presented in Appendix A.

TABLE III-2
SUPPLEMENTAL BIOLOGICAL TREATMENT DATA SUMMARY

Plant Number	Sub-Category	Raw Waste Flow (mgd)	Raw Waste BOD5 (mg/ℓ)	Raw Waste COD (mg/ℓ)	Raw Waste TSS (mg/ℓ)	Treated Effluent BOD5 (mg/ℓ)	Treated Effluent COD (mg/ℓ)	Treated Effluent TSS (mg/ℓ)	Time Period
12015	D	NA	313	NA	NA	20	NA	NA	1/1/76 to 12/31/76
12022	AC	1.45	2,132	(a)	NA	111	(a)	85	5/31/78 to 6/30/79
12026	CD	0.096	1,932	3,259	20	33	248	42	1/5/83 to 12/28/83
12036	AD	1.43	1,119	NA	NA	11	122	24	4/1/83 to 4/1/84
12097	C	0.061	1,597	1,944	NA	68	158	17	11/1/78 to 11/30/79
12132	AC	1.04	2,916	6,825	NA	NA	1,201	NA	8/2/82 to 12/31/83
12236	C	NA	1,264	2,043	NA	128	489	104	1/1/81 to 12/31/83
12307	D	NA	NA	NA	NA	18	86	17	1/1/83 to 1/31/83
12459	C	0.053	NA	NA	NA	3.5	87	6	1/5/83 to 12/28/83
12462	A	0.155	NA	NA	NA	252	882	707	3/1/81 to 4/30/83
55555	C	0.177	1,618	2,312	360	33	NA	75	1/1/82 to 12/31/82

NA = Not available
(a) Plant does not use Standard Methods for the COD test.

TABLE III-3
EFFLUENT FILTER PERFORMANCE INFORMATION

Plant	Subcategory	BOD5 Influent (mg/l)	BOD5 Effluent (mg/l)	BOD5 Reduction %	COD Influent (mg/l)	COD Effluent (mg/l)	COD Reduction %	TSS Influent (mg/l)	TSS Effluent (mg/l)	TSS Reduction %	Time Period
11111	C	NA	NA	--	NA	NA	--	110	78	29	3/26/84 - 4/11/84
12053	D	24	10	58	97	84	13	25	8	68	2/16/82 - 2/11/83(a) 11/19/74 - 3/25/83(b)
12161	AC	26.9	25.7	4	NA	766	--	61.6	18.6	70	6/1/81 - 12/31/81
		30.4	29.7	2	NA	519	--	53	31	42	1/1/82 - 12/31/82
		23.6	24.8	--	NA	348	--	15	10	33	1/1/83 - 12/31/83
		--	--	--	278	270	3	--	--	--	8/25/84 - 11/20/84
12317	D	NA	5	--	33	17	48	19	6	68	1/1/83 - 12/31/83
33333 44444	D	2.54(c)	1.55(d)	--	63(c)	49(d)	--	17.7(c)	8.5(d)	--	8/1/83 - 11/26/83

NA = Not available
(a) Influent time period
(b) Effluent time period
(c) Microscreen influent not tested; flocculation, clarification, and final neutralization are between the secondary effluent and the microscreen unit influent.
(d) Microscreen effluent not tested; chlorination and post aeration are between the microscreen unit effluent and the final plant effluent.

TABLE III-4

LIST OF PRIORITY POLLUTANTS

I. METALS

- ANTIMONY
- ARSENIC
- BERYLLIUM
- CADMIUM
- CHROMIUM
- COPPER
- LEAD
- MERCURY
- NICKEL
- SELENIUM
- SILVER
- THALLIUM
- ZINC

II. MISCELLANEOUS

- ASBESTOS *
- CYANIDES

III. DIBENZO-P-DIOXINS AND DIBENZOFURANS

- 2,3,7,8-TCDD

IV. PURGEABLE

- 1,1,1-TRICHLOROETHANE
- 1,1,2,2-TETRACHLOROETHANE
- 1,1,2-TRICHLOROETHANE
- 1,1-DICHLOROETHANE
- 1,1-DICHLOROETHENE
- 1,2-DICHLOROETHANE
- 1,2-DICHLOROPROPANE
- 1,3-DICHLOROPROPYLENE
- 2-CHLOROETHYL VINYL ETHER
- ACROLEIN
- ACRYLONITRILE
- BENZENE
- BROMOFORM
- BROMODICHLOROMETHANE
- BROMOMETHANE
- CARBON TETRACHLORIDE
- CHLOROBENZENE
- CHLOROETHANE
- CHLOROFORM
- CHLOROMETHANE
- DIBROMOCHLOROMETHANE
- ETHYL BENZENE
- METHYLENE CHLORIDE
- TETRACHLOROETHENE
- TOLUENE
- TRANS-1,2-DICHLOROETHENE
- TRICHLOROETHENE
- VINYL CHLORIDE

V. EXTRACTABLE

A. PESTICIDES

1. ORGANOHALIDE

- 4,4'-DDD
- 4,4'-DDE
- 4,4'-DDT
- ALDRIN
- ALPHA-BHC
- BETA-BHC
- CHLORDANE
- DELTA-BHC
- DIELDRIN
- ENDOSULFAN I
- ENDOSULFAN II
- ENDOSULFAN SULFATE
- ENDRIN
- ENDRIN ALDEHYDE
- GAMMA-BHC
- HEPTACHLOR
- HEPTACHLOR EPOXIDE
- PCB-1016
- PCB-1221
- PCB-1232
- PCB-1242
- PCB-1248
- PCB-1254
- PCB-1260
- TOXAPHENE

B. SEMI-VOLATILES

1. ACIDS

- 2,4,6-TRICHLOROPHENOL
- 2,4-DICHLOROPHENOL
- 2,4-DIMETHYLPHENOL
- 2,4-DINITROPHENOL
- 2-CHLOROPHENOL
- 2-NITROPHENOL
- 4-NITROPHENOL
- DINITROCRESOL
- PENTACHLOROPHENOL
- PHENOL

2. BASES

- 1,2-DIPHENYLHYDRAZINE
- 2,4-DINITROTOLUENE
- 2,6-DINITROTOLUENE
- 3,3-DICHLOROBENZIDINE
- 4-BROMOPHENYL PHENYL ETHER
- 4-CHLORO-3-METHYLPHENOL
- 4-CHLOROPHENYL PHENYL ETHER
- BENZIDINE
- bis(2-CHLOROETHYL) ETHER
- bis(2-CHLOROISOPROPYL) ETHER

B. SEMI-VOLATILES

2. BASES

- DI-N-PROPYLNITROSAMINE
- FLUORENE
- ISOPHORONE
- N-NITROSODIMETHYLAMINE
- N-NITROSODIPHENYLAMINE
- NITROBENZENE
- PYRENE

3. NEUTRALS

a. PHTHALATES

- BIS(2-ETHYLHEXYL) PHTHALATE
- BUTYL BENZYL PHTHALATE
- DI-N-BUTYL PHTHALATE
- DI-N-OCTYL PHTHALATE
- DIETHYL PHTHALATE
- DIMETHYL PHTHALATE

b. POLYNUCLEAR AROMATIC

- 2-CHLORONAPHTHALENE
- ACENAPHTHENE
- ACENAPHTHYLENE
- ANTHRACENE
- BENZO (A) ANTHRACENE
- BENZO (A) PYRENE
- BENZO (B) FLUORANTHENE
- BENZO (GHI) PERYLENE
- BENZO (K) FLUORANTHENE
- CHRYSENE
- DIBENZO(A,H) ANTHRACENE
- FLUORANTHENE
- INDENO(1,2,3-CD) PYRENE
- NAPHTHALENE
- PHENANTHRENE

c. CHLORINATED HYDROCARBONS

- 1,2,4-TRICHLOROBENZENE
- 1,2-DICHLOROBENZENE
- 1,3-DICHLOROBENZENE
- 1,4-DICHLOROBENZENE
- bis(2-CHLOROETHOXY) METHANE
- HEXACHLOROBENZENE
- HEXACHLOROBUTADIENE
- HEXACHLOROCYCLOPENTADIENE
- HEXACHLOROETHANE

* NOT ANALYZED FOR SAMPLES COLLECTED.

b. PEDCo Reports. Concurrent with the efforts to profile the pharmaceutical manufacturing industry using the 308 Portfolio Survey, PEDCo studied the various manufacturing processes/steps used in the production of fermented, extracted, and synthesized pharmaceuticals.(1,2,3)

PEDCo examined industry data and identified those products that comprise the major areas of production for each of the three manufacturing subcategories (A, B, and C). Available literature describing the step-by-step procedures used in the production of each substance was reviewed and the priority pollutants used by the industry were identified. These pollutants are listed in Table III-5.

It was not practical to identify every priority pollutant that could be used, because of the limited scope of the PEDCo study, the size and complexity of the industry, and the myriad of products manufactured.

c. OAQPS Study. EPA's OAQPS published a document in December 1978 providing guidance on air pollution control techniques for limiting emissions of VOCs from the chemical synthesis subcategory (C) of the pharmaceutical industry.(6)

As part of this study, the PMA surveyed selected pharmaceutical plants to determine estimates of the 10 largest volume VOCs that each company purchased and the mechanism by which they leave the plant (i.e., sold as product, sewered, or emitted as an air pollutant).

Table III-6 presents a compilation of the survey results. Of the 26 responding companies, 25 indicated that the 10 VOCs used in the greatest quantities accounted for 80 to 100 percent of total plant use. The other company stated that the 10 VOCs used in the greatest quantities accounted for only 50 percent of total plant use. These 26 companies accounted for 53 percent of the domestic sales of ethical pharmaceuticals in 1975.

Included in the list of 46 compounds presented in Table III-6 are seven priority pollutants. These compounds are methylene chloride, toluene, chloroform, benzene, carbon tetrachloride, 1,1,1-trichloroethane, and 1,2-dichlorobenzene.

Table III-7 presents a summary and analysis of the data outlined in Table III-6. Priority pollutants represent approximately 28 percent of total VOC usage in the industry segment analyzed. However, priority pollutants represent only 13 percent of the total mass discharge of VOCs to the plant sewers.

Table III-7 also indicates that of the total quantity of all VOCs discharged, only a fraction (16.6 percent) is discharged via wastewater. The priority pollutant VOCs are discharged with the wastewater in an even lower proportion (9.6 percent).

TABLE III-5
SUMMARY OF PRIORITY POLLUTANT USE: PEDCo REPORTS

Priority Pollutants Identified As Used In:

Subcategory A[1]

benzene
chloroform
1,1-dichloroethylene
1,2-trans-dichloroethylene
phenol
copper
zinc

Subcategory B[2]

benzene
carbon tetrachloride
1,2-dichloroethane
chloroform
methylene chloride
phenol
toluene
cyanide
lead
mercury
nickel
zinc

Subcategory C[3]

benzene
carbon tetrachloride
chlorobenzene
chloroethane
chloroform
1,1-dichloroethylene
1,2-trans-dichloroethylene
methylene chloride
methyl chloride
methyl bromide
nitrobenzene
2-nitrophenol
4-nitrophenol
phenol
toluene
chromium
copper
cyanide
lead
zinc

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1 Reference No. 1
2 Reference No. 2
3 Reference No. 3

TABLE III-6

COMPILATION OF DATA SUBMITTED BY THE PMA FROM 26 MANUFACTURERS OF ETHICAL DRUGS: 1975 OAQPS STUDY

Type of VOC	Annual Purchase	Annual Disposition (metric tons)						Solvent Recovery
		Air Emissions	Sewer	Incineration	Contract Haul	Other Disposal**	Product	
Priority Pollutants								
benzene+	1,010	270	350	150	80	--	90	20,500
carbon tetrachloride	1,850	210	120	1,510	--	--	--	--
chloroform	500	280	23	--	175	17	--	1,210
o-dichlorobenzene	60	1	60	--	--	--	--	7,060
methylene chloride	10,000	5,310	455	2,060	2,180	--	5	73,400
toluene+	6,010	1,910	885	1,590	1,800	--	--	23,850
trichloroethane	135	135	--	--	--	--	--	--
Subtotal	19,565	8,116	1,893	5,310	4,235	17	95	126,020
ITD-Listed Nonconventional Pollutants								
acetone	12,040	1,560	2,580	4,300	770	--	2,210	40,760
dimethyl formamide+	1,630	1,350	60	380	120	--	--	5,100
1,4-dioxane	43	2	--	--	41	--	--	--
ethyl ether	280	240	12	--	30	--	--	110,800
freons	7,150	6	--	--	--	--	7,145	--
methyl ethyl ketone	260	170	30	60	--	--	--	6,460
methyl isobutyl ketone+	260	260	--	--	--	--	65	6,160
pyridine	3	--	3	--	--	--	--	--
Subtotal	21,666	3,588	2,685	4,740	961	--	9,420	169,280
Non-ITD-Listed Nonconventional Pollutants								
acetic acid	930	12	770	--	--	--	160	1,040
acetic anhydride	1,265	8	550	--	--	--	410	300
acetonitrile	35	30	6	--	--	--	--	125
amyl acetate	285	120	165	--	--	--	--	3,510
amyl alcohol+	1,430	775	--	--	0	--	9	76,900
Blendax (Amoco)	530	--	--	--	--	--	530	--
butanol+	320	85	30	5	130	--	110	1,040
cyclohexylamine	3,930	--	--	--	--	--	3,930	--
diethylamine	50	50	3	--	--	--	--	300
diethyl carbonate	30	1	20	--	--	--	7	--
diethyl-ortho formate	54	--	21	--	--	--	33	--
dimethylacetamide	95	7	--	--	90	--	--	--
dimethylsulfoxide	750	4	210	535	--	--	--	4,760
ethanol	13,230	1,250	785	915	200	--	10,000	7,570
ethyl acetate	2,380	710	1,110	480	80	--	--	715
ethyl bromide	45	--	45	--	--	--	--	7,170
ethylene glycol	60	--	60	--	--	--	--	60
formaldehyde	30	5	20	--	--	--	1	--
formamide	440	--	290	--	110	--	30	--
hexane+	530	120	--	100	475	--	--	25,670
isobutyraldehyde	85	40	40	--	--	--	--	145
isopropanol+	3,850	1,000	1,130	1,150	470	25	3,090	3,880
isopropyl acetate	480	105	45	230	--	--	--	1,840
isopropyl ether	25	12	12	--	--	--	--	12
methanol	7,960	2,480	3,550	1,120	410	30	340	--
methyl cellosolve	195	90	100	--	--	--	--	360
methyl formate	415	--	310	--	50	--	60	1,130
polyethylene glycol 600	3	--	--	--	--	--	3	--
skelly solvent B	1,410	410	23	980	--	--	--	90
tetrahydrofuran	4	--	--	4	--	--	--	--
xylene+	3,090	170	510	1,910	140	--	3	9,400
Subtotal	43,936	7,484	9,805	7,429	2,155	55	18,716	146,017
Totals	85,167	19,188	14,383	17,479	7,351	72	28,231	441,317

Notes

Source - 26 member companies of the PMA reported these data which they felt represented 85 percent of the VOCs used in their operations; these reporting companies accounted for approximately 53 percent of the 1975 domestic sales of ethical pharmaceuticals.

**Deepwell or landfill.

+Annual disposition does not closely approximate annual purchase.

TABLE III-7
SUMMARY OF VOC EMISSION DATA: 1975 OAQPS STUDY

	Priority Pollutants (total of 7)	ITD-Listed Non-Conventional Pollutants (total of 8)	Non-ITD-Listed Nonconventional Pollutants (total of 31)	Total Compounds (total of 46)
Amount purchased (metric tons)	19,565	21,666	43,936	85,167
Amount discharged (metric tons)	19,666	21,394	45,644	86,704
Amount recovered within the plant (metric tons)	126,020	169,280	146,017	441,317
Total amount used in plant (sum of items 1 and 3; metric tons)	145,585	190,946	189,953	526,484
Percent recovered	86.6	88.7	76.9	83.8
Percent of total used that is discharged	13.5	11.2	24.0	16.5
Percent of total used that is discharged to sewer	1.3	1.4	5.2	2.7
Percent of total discharged that is discharged to sewer	9.6	12.6	21.5	16.6

OAQPS again worked with the PMA in 1986 to update purchase and disposition data for seven VOCs used in pharmaceutical manufacturing processes.(7) The seven VOCs included in the survey are carbon tetrachloride, chloroform, ethylene dichloride, ethylene oxide, methylene chloride, perchloroethylene, and trichloroethylene.

Results from the 22 firms that responded to the survey are summarized in Table III-8. The PMA indicated that the responding firms represent approximately 70 percent of U.S. pharmaceutical sales for 1985.

d. RSKERL/ADA Study. RSKERL/ADA conducted an applied research study entitled, "Industry Fate Study," for the Effluent Guidelines Division (now the ITD).(8) The purpose of this report was to determine the fate of specific priority pollutants as they pass through a biological treatment system. In the study, priority pollutants associated with the manufacture of pharmaceuticals at two industrial facilities were identified. Results of these wastewater analyses are reported in Appendix B. RSKERL/ADA data are limited since they are from only two plants; however, they do supplement the other data.

e. Total Toxic Volatile Organics (TTVOs) Questionnaire. To determine the extent to which the wastewater of indirect-discharging pharmaceutical plants was contaminated by TVOs, EPA sent 308 Questionnaires to nine indirect-discharging plants which had indicated the use of TVOs. EPA also sent questionnaires to six other plants that had commented on the proposed pretreatment standard for TTVOs (see 47 FR 53585, November 26, 1982). EPA sought information on wastewater contamination by TVOs to develop plant-by-plant cost estimates for steam-stripping technology. A copy of the questionnaire sent to the participating pharmaceutical plants is in Section 22-6-1 of the record supporting the 1983 rulemaking efforts.

Questionnaire responses were received from 16 plants (one company responded for another plant not sent a questionnaire). Five plants reported contamination of part of their process wastestream by one or more TVOs at concentrations greater than 10 mg/. A summary of the priority pollutant data obtained from the questionnaire is presented in Table III-9. The median percentage of process wastewater contaminated by TVOs was 26 percent at the five plants. This percentage was used to develop plant-by-plant steam-stripping costs (see Appendix A of the Final Development Document).

f. State and Local Data. State and local data presented in Appendix C verify that several volatile hazardous constituents are present in wastewater discharged to POTWs from pharmaceutical manufacturing facilities. Specifically, high average concentrations are shown for acetone (9.65 mg/l), toluene (2.84 mg/l), and xylene (1.0 mg/l).

TABLE III-8

DATA SUBMITTED BY PMA
FROM 22 PHARMACEUTICAL MANUFACTURERS
1985 OAQPS STUDY

Type of VOC	Annual Purchase	Annual Disposition (metric tons) Air Emissions	Sewer	Incineration	Contract Haul	Other Disposal*	Product
carbon tetrachloride	13	12	--	--	--	--	--
chloroform	686	261	124	91	67	132	1.4
ethylene dichloride	1,111	125	41	833	79	--	--
ethylene oxide	9,587	34	6.7	1	2.5	--	9,508[1]
methylene chloride[2]	1,539	1,031	118	62	154	113	41
perchloroethylene	6.5	--	--	2	--	--	2.3
trichloroethylene	2	--	--	2	--	--	--
Totals	14,054.5 [SIC]	1,462	289.7	991	302.5	245	9,552.7

Source - Data are from a letter to OAQPS from PMA. Data represent estimates for 1985 use and disposition. 22 PMA member firms responded, representing approximately 70% of pharmaceutical sales for 1985.

[1]Ethylene oxide use is primarily as a reactant in pharmaceutical manufacturing processes; that is, converted into drug product.

[2]Data for methylene chloride do not include figures already submitted from 9 of the reporting firms. (Estimated to be 13,700 metric tons).

*Other disposal modes: fractional dilution; off-site recovery; deep well; conversion; and solvent recovery.

TABLE III-9
SUMMARY OF PRIORITY POLLUTANT DATA
FROM THE 1983 TTVO QUESTIONNAIRE

Plant	Compound	Wastewater Concentration: Undiluted Process (µg/ℓ)	Wastewater Concentration: Discharge to POTW (µg/ℓ)	Manufacturing process
12003	chloroform	--	1,843(a)	C
	methylene chloride	--	18,591(a)	C
	toluene	--	1,921(a)	C
12057	carbon tetrachloride	0	--	C
	1,2-trans-dichloroethylene	0	--	C
	methylene chloride	0	--	C
	toluene	0	--	C
12107(b)				
12112(c)	benzene	21,000	--	D
	carbon tetrachloride	6,000	--	D
	chlorobenzene	7,000	--	D
	chloroform	6,000	--	D
	1,2-dichlorobenzene	3,000	--	D
	1,2-dichloroethane	5,000	--	D
	methylene chloride	32,000	--	D
	toluene	21,000	--	D
	1,2,4-trichlorobenzene	3,000	--	D
	trichloroethylene	200	--	D
12123	bis(2-chloroethoxy)methane	50	--	C
	chloroform	<50	--	C
	cyanide	<50	--	C
	1,2-dichloroethane	<10	--	C
	ethylbenzene	<30	--	C
	ethyl chloride	--	--	--
	methylene chloride	2,600	--	C
	toluene	3,400	--	C
12168	toluene	500,000	--	C
12252	chloroform	4,800	640	C
	methylene chloride	6,500	859	C
	toluene	6,200	819	C
12254	chloroform	60,000	--	A,C
	methylene chloride	5,000	--	C

TABLE III-9 (continued)

Plant	Compound	Wastewater Concentration: Undiluted Process, (µg/ℓ)	Wastewater Concentration: Discharge to POTW (µg/ℓ)	Manufacturing process
12257	carbon tetrachloride	--	nd	C
	1,2-dichloroethane	--	nd	C
	chloroform	--	12	C
	methylene chloride	--	nd	C,D
	toluene	--	nd	C
12275	acetone	--	5-414	
	bromoform	--	0-139	
	chlorobenzene	--	112-190	C
	chloroform		39-55	
	dichlorobromomethane	--	0-14	
	1,2-dichloroethane	--	32-48	C
	methylene chloride	--	0	C
	2,2,2'-oxybispropane	--	0-552	
	1-propyl alcohol	--	0-12	
	1-propyl acetate	--	0-10	
	toluene	--	431-1090	C
	cyanide	--	--	C
12310(d)				
12330	methylene chloride	20,000,000	45,000	D
12339(e)				
12447(f)	methylene chloride	--	--	A
	toluene	--	--	C
12477	chlorobenzene	0	--	C
	chloroform	3,000	--	B,C
	methylene chloride	72,000	--	C
	toluene	203,000	--	C

TABLE III-9 (continued)

Plant	Compound	Wastewater Concentration: Undiluted Process (µg/ℓ)	Wastewater Concentration: Discharge to POTW (µg/ℓ)	Manufacturing process
12481	methylene chloride	0	--	D
20349(g)				

-- Data not available.
(a) Flow-weighted average of 19 24-hour composite samples.
(b) Process wastewater does not contain volatile priority pollutants.
(c) This plant no longer produces pharmaceuticals. However, data shown are from a a period when pharmaceuticals were manufactured at this plant.
(d) This facility does not engage in manufacturing activities.
(e) No wastewater at this facility is discharged to a POTW.
(f) Methylene chloride and toluene discharged during production of certain products; see questionnaire.
(g) This facility does not use or produce any TTVOs.
nd Not detected.

g. Screening and Verification Sampling Programs. Information on priority pollutants from the previously mentioned reports and surveys was largely qualitative. Moreover, the earlier reports did not always distinguish between pollutants used by a plant and those found in the final effluent. Beginning in 1978, EPA initiated the Screening and Verification Sampling Program, in which a number of plants representing the pharmaceutical manufacturing industry were sampled for priority pollutants and traditional pollutants (BOD_5, COD, and TSS) in a two-phase program. The first phase, called the screening phase, involved 26 plants and covered a broad cross section of the industry. This was followed by a verification phase which limited the sampling to only five carefully selected plants. Augmentation of the existing data base with analytical results of the Screening and Verification Sampling Program, along with the qualitative information from other data-gathering efforts, provided EPA with information used to characterize the industry's wastewater.

The screening program was conducted to determine the presence or absence of priority pollutants in the wastewater of a number of pharmaceutical plants, and to quantify those present. The information was then used to limit the search to specific priority pollutants for the verification program and to identify plants likely to provide information to accurately characterize industry wastewater.

Major processing areas and subcategory coverage, range of wastewater flows, and an assortment of both in-plant and EOP treatment technology/techniques were used as selection criteria for the screening plants. Multiple subcategory plants, as well as plants within only one subcategory, were deliberately sought. Similarly, EPA made a special effort to include plants with wastewater flows less than 100 gpd and more than 2.5 mgd. Descriptions of the plants and sampling points are presented in Appendix O of the Proposed Development Document.

Included in the screening group were nine direct dischargers, seven indirect dischargers, three zero dischargers, and seven plants that used more than one mode of discharge. In the latter group, three plants were both indirect and zero dischargers, three were both direct and zero dischargers, and one used all three modes of discharge. The screening plants with subcategory designations are as follows:

Plant ID No.	Subcategory	Plant ID No.	Subcategory
12015	D	12210	BC
12022	AC	12231	AD
12026	C	12236	C
12036	A	12248	D
12038	ABCD	12256	ABCD
12044	AD	12257	ABCD
12066	BCD	12342	ACD
12097	CD	12411	BCD

Plant ID No.	Subcategory	Plant ID No.	Subcategory
12108	ACD	12420	BD
12119	AB	12439	CD
12132	AC	12447	ABCD
12161	CD	12462	A
12204	ABCD	12999	CD

The verification program was developed to confirm the presence of the priority pollutants identified by the screening program and to provide quantitative pollutant data with known precision and accuracy. The analytical results from these episodes serve as a basis to confirm the presence of the pollutants of interest, as well as to identify effective control and treatment technologies for these pollutants.

Selection of the five plants for the verification program was based in part on general criteria presented in Section II of the Proposed Development Document. A criterion mentioned earlier, and which weighed heavily in the final selection process, was the assortment of major priority pollutants being used as raw materials for the manufacture of pharmaceuticals. Table III-10 lists the priority pollutants that appear in the wastestreams at detectable levels at each of the screening plants. Other plant-specific characteristics that were considered in the final selection process are summarized in the following paragraphs on a plant-by-plant basis.

Plant 12411. Three of the common priority pollutants used by the industry were found in the wastestreams of Plant 12411: methylene chloride, chloroform, and toluene. The presence of these pollutants, a process area involving three subcategories, use of a solvent recovery system, and pretreatment of wastewater followed by aerated lagoon treatment justified this plant for verification sampling.

Plant 12038. This plant was selected for sampling in the verification program because it used potential BAT technology, including steam-stripping, aerobic biological treatment, and thermal oxidation. The presence of several priority pollutants (including nitrosamines), the existence of a large historical data base relating to nitrosamines, and the inclusion of both pesticides and pharmaceuticals in the manufacturing operations at the plant were also considered in the selection process.

Plant 12236. Limitation to one subcategory, reported flows of about 0.81 mgd, use of cyanide as raw material, and treatment of wastewater by the activated sludge process qualified this plant for the verification program. Also of interest was the use of in-plant treatment processes, including cyanide destruction and solvent recovery.

TABLE III-10
SUMMARY OF PRIORITY POLLUTANT OCCURRENCE SCREENING PLANT DATA

Compound	Number of Occurrences Detected Influent (25)*	Detected Effluent (20)*	Above 500 ug/l in Effluent(20)*	Max. Effluent Level ug/l
acenaphthene	4 (16%)			
benzene	15 (60%)	3 (15%)		120
benzidine	1 (4%)			
carbon tetrachloride	3 (12%)	1 (5%)		16
chlorobenzene	5 (20%)			
1,2-dichloroethane	5 (20%)	4 (20%)	1	500
1,1,1-trichloroethane	8 (32%)	4 (20%)		33
1,1-dichloroethane	4 (16%)			
1,1,2-trichlorethane	4 (16%)	1 (5%)		14
chloroethane	2 (8%)			
bis(2-chloroethyl)ether	1 (4%)	1 (5%)		20
2,4,6-trichlorophenol	1 (4%)			
chloroform	16 (64%)	9 (45%)		110
2-chlorophenol	1 (4%)			
1,2-dichlorobenzene	2 (8%)			
1,4-dichlorobenzene	1 (4%)			
1,1-dichloroethylene	5 (20%)	2 (10%)		180
1-2-trans-dichloroethylene	1 (4%)			
2-4-dimethylphenol	1 (4%)	1 (5%)		15
2-4-dinitrotoluene	2 (8%)	1 (5%)		14
2-6-dinitrotoluene	1 (4%)			
1,2-diphenylhydrazine	1 (4%)			
ethylbenzene	12 (48%)	2 (10%)		160
fluoranthene	1 (4%)			
bis(2-chloroisopropyl) ether	3 (12%)	2 (100%)		
methylene chloride	17 (68%)	15 (75%)	2	2600
methyl chloride	1 (4%)			
methyl bromide	1 (4%)			
bromoform	1 (4%)	1 (5%)		44
isophorone	2 (8%)			
napthalene	1 (4%)			
nitrobenzene	1 (4%)			
2-nitrophenol	3 (12%)			
4-nitrophenol	3 (12%)	1 (5%)		15
4,6-dinitro-o-cresol		1 (5%)		15
N-nitrosodiphenylamine	1 (4%)			
pentachlorophenol	2 (8%)			
phenol	14 (56%)	4 (20%)		120
bis(2-ethylhexyl) phthalate	10 (40%)	8 (40%)		68

TABLE III-10 (continued)
SUMMARY OF PRIORITY POLLUTANT OCCURRENCE SCREENING PLANT DATA

Compound	Number of Occurrences Detected Influent (25)*	Detected Effluent (20)*	Above 500 ug/l in Effluent(20)*	Max. Effluent Level ug/l
butyl benzyl phthalate	2 (8%)			
di-n-butyl phthalate	3 (12%)	4 (20%)		15
diethyl phthalate	1 (4%)	1 (5%)		20
anthracene	2 (8%)			
fluorene	1 (4%)			
phenanthrene	1 (4%)			
tetrachloroethylene	4 (16%)	2 (10%)		18
toluene	16 (64%)	5 (25%)	1	1350
trichloroethylene	3 (12%)	2 (10%)		11
antimony (total)	10 (40%)	3 (15%)		90
arsenic (total)	5 (20%)	3 (15%)		30
beryllium (total)	4 (16%)	2 (10%)		2.0
cadmium (total)	8 (32%)	5 (25%)		40
chromium (total)	23 (92%)	15 (75%)		304
copper (total)	24 (96%)	16 (80%)		63
cyanide (total)	11 (44%)	10 (50%)		7700
lead (total)	13 (52%)	9 (45%)		400
mercury (total)	16 (64%)	12 (60%)		1.58
nickel (total)	14 (56%)	9 (45%)		310
selenium (total)	7 (28%)	3 (15%)		56
silver (total)	7 (28%)	3 (15%)		40
thallium (total)	5 (20%)	4 (20%)		29
zinc (total)	21 (84%)	17 (85%)		403

* Indicates number of plant streams

Plant 12026. Plant 12026 is a single subcategory (C) plant with a reported flow of 0.101 mgd. A treatment train consisting of activated sludge, an aerated lagoon, and a polishing pond after in-plant treatment by solvent recovery were the reasons this plant was selected for verification sampling.

Plant 12097. Plant 12097 is a multiple subcategory (CD) plant with a reported flow of 0.035 mgd. The use of cyanide in production, in-plant solvent recovery, and an activated sludge treatment system were considered in selecting this plant.

A plant-by-plant summary of analytical results from the sampling program is presented in Appendix G of the Proposed Development Document.(5)

Table III-11 lists the conventional, nonconventional, and priority pollutants that were identified and the frequency at which they were found in the wastestream. Although a number of priority pollutants appeared in the wastestream, only a few were sufficiently repetitive to cause concern. Pesticides and PCBs detected in one plant's effluent are not believed to be due to pharmaceutical-related activity.

Wastewater entering and leaving the EOP wastewater treatment train were among those wastestreams sampled in this program. Concentration levels for many of the priority pollutants in the final effluent are relatively low because of (1) in-plant treatment and process controls to minimize specific wastewater pollution, (2) dilution of concentrated process wastewater with other less concentrated wastewater, and (3) incidental removal of some specific chemical pollutants by EOP treatment.

h. Pharmaceutical/POTW Sampling. A six-day sampling episode was conducted concurrently at Plant 12342 and the POTW which treats its wastewater in May 1983.(9) The purpose of the sampling was to define and document the mass of toxic pollutants discharged from a major pharmaceutical facility and to monitor the fate and treatability of these toxic pollutants at the POTW treating the wastewater. Sampling results were evaluated for the possible "pass-through" of toxic pollutants to the receiving water and the interference of treatment processes by the toxins which, in either situation, would support the recommendation for toxic pollutant pretreatment standards for the industry. Plant 12342, on average, discharges about 1 mgd of solvent-laden wastewater. This wastestream combines with approximately 79 mgd of residential, commercial, and industrial sewage before being treated at the POTW. The POTW is a well-maintained and properly operated secondary treatment facility which uses the activated sludge process. Average BOD_5 and TSS effluent concentrations were 12 and 24 mg/l, respectively, during the most recent 12-month period prior to the sampling episode. Plant 12342 effluent concentrations of methylene

TABLE III-11

SUMMARY OF PRIORITY POLLUTANT CONCENTRATIONS
SCREENING/VERIFICATION DATA BASE

Priority Pollutant	Influent (µg/ℓ)						Effluent (µg/ℓ)					
	Number of Plants	Number of Observations	Minimum	Maximum	Median	Mean	Number of Plants	Number of Observations	Minimum	Maximum	Median	Mean
Volatile Organics												
acrolein	0	0	--	--	--	--	1	1	100	100	100	100
benzene	11	19	15	10,300	120	1,586	1	1	120	120	120	120
bromoform	1	2	12	12	1.2	12	0	0	--	--	--	--
carbon tetrachloride	3	5	12	300	18	81	2	2	16	61	39	39
chlorobenzene	4	6	11	123,000	3,206	36,405	0	0	--	--	--	--
chloroform	14	22	26	1,620	170	396	6	7	14	150	90	79
1,2-dichloroethane	8	17	12	14,000	62	2,516	5	9	22	500	62	158
1,1-dichloroethylene	1	1	230	230	230		1	1	180	180	180	180
1,3-dichloropropylene	1	1	100	100	100	100	0	0	--	--	--	--
ethylbenzene	9	18	11	42,000	24	3,237	3	3	14	22	17	18
methylene chloride	18	31	16	200,000		11,356	14	21	12	8,100	120	863
methyl chloride	2	4	59	13,000	8,600	7,565	2	4	100	410	310	283
1,1,1-trichloroethane	8	11	17	1,300	22	169	4	6	10	33	20	21
1,1,2-trichloroethane	2	2	19	20	20	20	0	0	--	--	--	--
trichlorofluoromethane*	1	1	970	970	970	970	1	1	420	420	420	420
1,1,2,2-tetrachloroethane	1	1	20	20	20	20	0	0	--	--	--	--
tetrachloroethylene	8	4	14	36	31	28	1	1	18	18	18	18
toluene	14	29	50	227,000	310	21,075	4	4	100	315	185	196
trichloroethylene	2	2	11	124	68	68	1	1	14	14	14	14
vinyl chloride	1	1	14	14	14	14	0	0	--	--	--	--

TABLE III-11 (continued)

Priority Pollutant	Influent (µg/ℓ)						Effluent (µg/ℓ)					
	Number of Plants	Number of Observations	Minimum	Maximum	Median	Mean	Number of Plants	Number of Observations	Minimum	Maximum	Median	Mean
Semivolatile Organics												
acenaphthene	2	2	35	92	64	64	0	0	--	--	--	--
anthracene	1	1	14	14	14	14	0	0	--	--	--	--
bis(2-chloroisopropyl) ether	2	2	300	448	374	374	1	1	181	181	181	181
bis(2-ethylhexyl) phthalate	8	10	10	760	105	157	6	9	10	68	30	36
butyl benzyl phthalate	3	3	12	719	18	250	0	0	--	--	--	--
2-chlorophenol	1	1	50	50	50	50	0	0	--	--	--	--
1,2-dichlorobenzene	2	2	12	20	16	16	0	0	--	--	--	--
1,4-dichlorobenzene	1	1	90	90	90	90	0	0	--	--	--	--
2,4-dichlorophenol	1	1	10	10	10	10	0	0	--	--	--	--
diethyl phthalate	1	1	61	61	61	61	2	2	10	20	15	15
2,4-dimethylphenol	1	1	62	62	62	62	1	1	15	15	15	15
di-n-butyl phthalate	4	4	18	20	20	19	2	2	10	15	13	13
4,6-dinitro-o-cresol	1	1	15	15	15	15	0	0	--	--	--	--
2,4-dinitrotoluene	1	1	68	68	68	68	0	0	--	--	--	--
fluorene	1	1	27	27	27	27	1	1	10	10	10	10
isophorone	2	2	11	1,014	513	513	0	0	--	--	--	--
2-nitrophenol	2	2	23	119	71	71	0	0	--	--	--	--
4-nitrophenol	2	2	181	1,600	891	891	1	1	15	15	15	15
N-nitrosodiphenylamine	1	1	12	12	12	12	0	0	--	--	--	--
pentachlorophenol	2	2	42	62	52	52	0	0	--	--	--	--
phenanthrene	1	1	14	14	14	14	0	0	--	--	--	--
phenol	20	36	12	51,000		7,529	9	12	10	126	23	47
2,4,6-trichlorophenol	1	1	20	20	20	20	0	0	--	--	--	--

TABLE III-11 (continued)

Priority Pollutant	Influent (µg/ℓ)						Effluent (µg/ℓ)					
	Number of Plants	Number of Observations	Minimum	Maximum	Median	Mean	Number of Plants	Number of Observations	Minimum	Maximum	Median	Mean
Metals												
antimony	8	9	12	210	27	45	2	5	20	51	31	34
arsenic	4	4	13	43	31	29	3	6	10	20	12	13
cadmium	4	5	10	40	32	25	1	1	40	40	40	40
chromium	18	30	13	650	39	117	13	21	10	304	27	77
copper	21	39	14	7,030		571	13	25	14	106	31	38
lead	9	13	14	500	63	119	9	14	13	400	33	64
mercury	16	31	0.1	0.1		3.9	11	19	0.1	1.3	0.7	0.7
nickel	11	19	15	630	39	103	8	16	19	300	51	83
selenium	4	5	16	60	28	31	2	5	12	56	45	42
silver	2	2	24	40	32	32	1	1	40	40	40	40
thallium	2	3	18	43	40	34	2	5	10	129	11	37
zinc	20	37	29	2,070		363	17	32	13	2,009	118	240
Other												
cyanide	8	16	18	540	140	153	6	11	30	7,700	100	827

* Deleted from the list of priority pollutants as per 46 CFR 2266.

chloride ranged from 13,400 to 166,000 mg/l during the sampling episode. The average effluent concentration of methylene chloride was 50,030 mg/l; the median concentration was 30,450 mg/l. On average, 85 percent of the methylene chloride mass in the POTW influent originates from Plant 12342. The average POTW methylene chloride influent concentration was 414 mg/l. The average secondary effluent methylene chloride concentration at the POTW was 177 mg/l; daily methylene chloride removals ranged from nine to 72 percent. Other toxic pollutants at detectable concentrations in the pharmaceutical effluent wastestream were phenol, isophorone, and toluene. These pollutants were reduced to much lower secondary effluent levels than methylene chloride at the POTW. Analytical results for the six-day sampling episode at Plant 12342 are summarized in Table III-12.

Additional analytical data characterizing the wastewater from Plant 12342 with respect to VOCs were supplied by the local POTW. In their comments on EPA's November 26, 1982, proposed regulations, POTW officials provided a summary of the sampling and analysis done of Plant 12342 wastewater. The data indicate that Plant 12342 is a significant source of acetone, methanol, methylene chloride, and MIBK. A summary of the sampling, and analysis of data collected by the POTW, is presented in Table III-13.

C. NEW DATA SOURCES

EPA recently undertook additional qualitative and quantitative data collection programs, to more fully evaluate the extent to which hazardous constituents are being discharged to POTWs from pharmaceutical manufacturing facilities.

Results of the qualitative assessment of priority and hazardous nonconventional pollutant solvent usage by the industry (based on a review of product patents) and the sampling and analysis program conducted at six pharmaceutical manufacturing facilities are discussed in the following paragraphs.

1. Product Patent Review

Most processes used to produce pharmaceuticals contribute a variety of volatile organic solvents to industry wastewater. Previous research conducted by EPA characterized the industry's use of priority pollutant solvents and extractive agents through a review of literature and product patents.(1,2,3) Because EPA's list of pollutants of concern expanded beyond the list of priority pollutants to include those on the ITD List of Analytes, a follow-up review of pharmaceutical product patents was conducted to determine which ITD-listed VOCs are likely being used as solvents and/or extractive agents by the industry and, therefore may be in the industry wastewater.

TABLE III-12
SUMMARY OF ANALYTICAL DATA
PLANT 12342

Pollutant	Day 1 (µg/ℓ)	Day 2 (µg/ℓ)	Day 3 (µg/ℓ)	Day 4 (µg/ℓ)	Day 5 (µg/ℓ)	Day 6 (µg/ℓ)
Volatile Organics						
methylene chloride	13,400	37,600	166,000	32,800	22,300	28,100
toluene	--	--	--	620	--	5,200
Semivolatile Organics						
1,2-dichlorobenzene	--	--	--	--	--	--
1,4-dichlorobenzene	--	--	--	--	--	--
isophorone	3.9	2.2	3.2	2.1	2.9	4.1
naphthalene	6.9	5.2	7.0	6.3	8.9	6.6
phenol	3,240	4,540	3,320	2,340	2,560	4,090
Metals and Cyanide						
chromium	--	40	40	40	40	40
copper	--	100	--	100	--	--
cyanide	50	30	40	30	30	20
mercury	0.4	0.5	0.2	0.4	0.2	0.4
zinc	80	300	320	360	1,160	600
Nonconventional Metals						
aluminum	--	1,300	1,200	800	1,000	800
barium	--	50	--	--	--	--
boron	200	100	--	--	--	--
calcium	126,000	146,000	151,000	183,000	134,000	156,000
iron	100	2,250	2,400	1,800	2,200	1,900
magnesium	21,000	30,900	34,800	39,400	31,600	33,400
manganese	100	250	200	300	300	200
sodium	109,000	1,118,000	587,000	831,000	692,000	627,000

Parameters not listed were not detected above the analytical detection limit.
-- = Not detected.

TABLE III-13
SUMMARY OF ANALYTICAL DATA
SUBMITTED BY THE LOCAL POTW
FOR PLANT 12342

Sample Date	Flow (mgd)	Methanol (µg/ℓ)	Acetone (µg/ℓ)	MIBK (µg/ℓ)	Methylene Chloride (µg/ℓ)	Chloroform (µg/ℓ)	1,2-Dichloro-ethane (µg/ℓ)	1,1,1-Tri-chloroethane (µg/ℓ)	Trichloro-ethylene (µg/ℓ)	Tetrachloro-ethylene (µg/ℓ)
4/19/82	0.920	70,000	180,000	40,000	46,000	780	<10	<10	<10	250
4/20/82	0.948	45,000	240,000	110,000	89,000	160	<10	<10	<10	<10
4/21/82	0.731	560,000	510,000	270,000	65,000	2,600	<100	<100	<100	<100
4/22/82	0.813	110,000	550,000	120,000	32,000	160	<100	<100	<100	<100
4/23/82	0.761	120,000	190,000	50,000	180,000	320	<100	<100	<100	<100
4/24/82	0.772	540,000	800,000	55,000	830,000	<100	<100	<100	<100	<100
4/25/82	0.773	50,000	120,000	50,000	360,000	<100	<100	<100	<100	<100
7/27/82	0.864	46,000	68,000	49,000	8,100	150	<10	<15	19	8
7/28/87	0.787	91,000	910,000	26,000	6,200	280	<10	<15	14	9
8/3/82	0.665	510,000	83,000	24,000	24,000	180	<10	<15	10	18
8/24/82	0.810	240,000	57,000	18,000	5,200	<10	<10	<10	<10	<10
8/25/82	0.865	170,000	180,000	<15,000	3,400	20	<10	<10	<10	<10
3/9/82	N/A	N/A	N/A	N/A	8,800	570	<100	<100	<100	<100

a. Identification of Patents. With the aid of the 1983 Merck Index (10), 729 U.S. Patents were identified as being associated with the manufacture of the 1,311 Subcategory A, B, and C products in EPA's data base. Patent information was found for 59 percent of Subcategory A products, 14 percent of Subcategory B products, and 42 percent of Subcategory C products. Figure III-1 summarizes information on the extent of patent coverage.

b. Identification of Volatile Organic Solvents of Interest. Each product patent was reviewed to determine which, if any, of the 89 VOCs listed in Table III-14 may be used as a solvent or extractive agent in the manufacture of that product. The list of 89 VOCs is a compilation from two sources: (1) the ITD List of Analytes (see Appendix D); and (2) the DSS List of Pollutants (see Appendix E).

c. Results. Results of the patent search indicate that 43 of the 89 VOCs reviewed are possibly being used in the manufacture of pharmaceuticals. Eleven of the 43 VOCs identified are priority pollutants. Table III-15 shows the subcategory in which the 43 compounds are likely to be used. Figure III-2 summarizes the number of products in which any of the 43 VOCs may be used in their manufacture. This information should be a good indicator of the solvents most commonly used in Subcategory A, B, and C manufacturing operations.

Results of the patent review also indicate that a significant portion of the plants manufacturing Subcategory A, and/or B, and/or C products are potentially using one or more of the listed solvents. Sixteen of a possible 31 direct-discharging plants (52 percent), 59 of a possible 131 indirect-discharging plants (45 percent), and 11 of a possible 33 zero dischargers (33 percent), are possibly using one or more of the listed solvents. Information on the number of products at each plant that may use any of the 43 VOCs in their manufacture is presented in Appendix F.

d. Discussion. Some insight on the accuracy of the patent review method to identify nonconventional pollutant VOCs being used in process operations, and which plants are most likely using them, can be obtained by reviewing the accuracy of the patent search process to identify plants known to be using priority pollutant solvents. Table III-16 summarizes the number of products that each Subcategory A, and/or B, and/or C facility manufacturers that may use a given priority pollutant solvent, according to patent information. The number of products is enclosed in parentheses if available 308 Portfolio Survey information indicates they actually do use or have used that compound as a raw, intermediate, or final material in pharmaceutical product manufacture.

The following general observations can be made based on a comparison of the predicted (based on patent review) and actual (based on 308 Portfolio) solvent use information for priority pollutants contained in Table III-16.

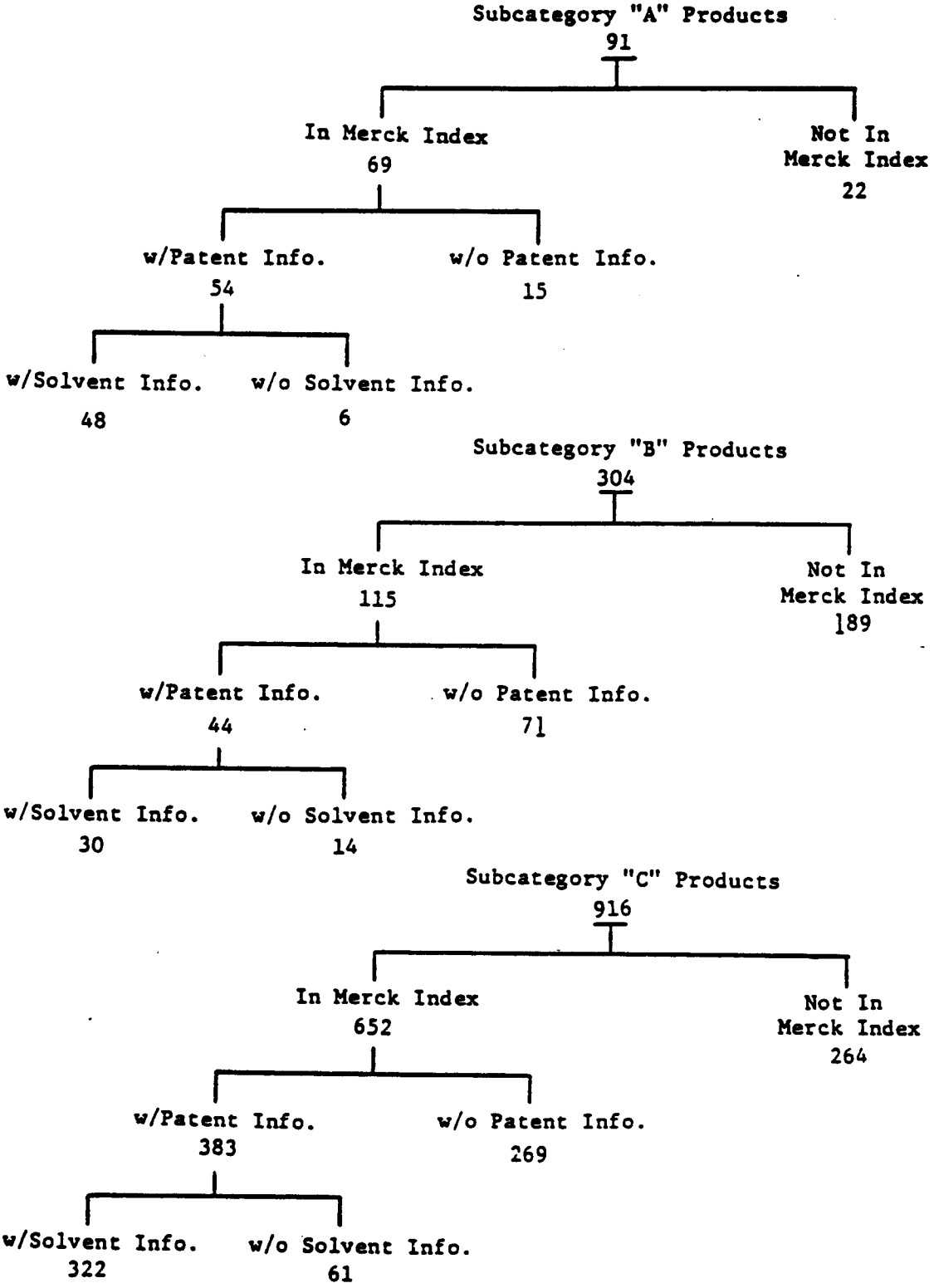


Figure III-1. Product Patent Coverage

TABLE III-14
ITD AND/OR DSS LISTED VOLATILE ORGANIC COMPOUNDS
REVIEWED FOR MENTION IN
PHARMACEUTICAL PRODUCT PATENTS

Compound Name	Common Name	Source
acetaldehyde		(b)
acetonitrile		(a,b)
acetophenone		(a,b)
acetyl chloride		(b)
acrylonitrile		(a,b)
aniline		(b)
benzene		(a,b)
bromodichloromethane	dichlorobromoethane	(a)
bromomethane	methyl bromide	(a,b)
2-butanone (MEK)	methyl ethyl ketone	(a,b)
carbon disulfide		(a,b)
chlorobenzene		(a,b)
chloroethane		(a,b)
2-chloroethylvinyl ether		(a)
chloroform		(a,b)
chloromethane		(a,b)
3-chloropropene	allyl chloride	(a)
3-chloropropionitrile	3-chloropropanenitrile	(a)
cumene		(b)
cyclohexane		(b)
dibromochloromethane		(a)
1,2-dibromoethane	ethylene dibromide	(a)
dibromomethane	methylene bromide	(a,b)
dichlorodifluoromethane		(a,b)
1,1-dichloroethane		(a,b)
1,2-dichloroethane		(a,b)
1,1-dichloroethene	1,1-dichloroethylene	(a,b)
1,2-dichloroethylene		(b)
1,2-dichloropropane		(b)
1,3-dichloro-2-propanol		(a,b)
cis-1,3-dichloropropene		(a)
diethyl ether		(a,b)
dimethyl sulfoxide		(a)
dimethylamine		(b)
1,4-dioxane	p-dioxane	(a,b)
epichlorohydrin		(b)
ethanol, 2-chloro	ethylene chlorohydrin	(a)
ethyl acetate		(b)
ethylbenzene		(a,b)
ethyl cyanide	propionitrile	(a)
ethyl methacrylate		(a)
ethylene oxide	oxirane	(a)

TABLE III-14 (Continued)

Compound	Common Name	Source
formaldehyde		(a,b)
formic acid		(a,b)
furan		(b)
furfural		(b)
2-hexanone		(a)
hydrazine		(b)
iodomethane	methyl iodine	(a)
isobutyl alcohol		(a)
methanol	methyl alcohol	(b)
methyl mercaptan	methanthiol	(b)
methyl methacrylate		(a)
methyl methanesulfonate	methylsulfonic acid	(a)
4-methyl-2-pentanone	MIBK	(a,b)
methylene chloride	dichloromethane	(a,b)
N-butyl alcohol		(b)
2-nitropropane		(b)
N-nitrosodiethylamine		(a)
N-nitrosomethylethylamine		(a)
propanedinitrile		(a)
2-propanone	acetone	(a,b)
2-propen-1-ol		(a)
2-propenal	acrolein	(a,b)
2-propenenitrile,2-methyl	methacrylonitrile	(a)
2-propyn-1-ol	propargyl alcohol	(a)
pyridine		(a,b)
resorcinol		(a)
styrene		(b)
1,1,1,2-tetrachloroethane		(a,b)
1,1,2,2-tetrachloroethane		(a,b)
tetrachloroethene	trichloroethylene	(a,b)
tetrachloromethane	carbon tetrachloride	(a,b)
tetrahydrofuran		(b)
toluene		(a,b)
total xylenes	xylene	(a,b)
trans-1,2-dichloroethene		(a,b)
trans-1,3-dichloropropene		(a)
trans-1,4-dichloro-2-butene		(a)
tribomomethane	bromoform	(a)
1,1,1-trichloroethane		(a,b)
1,1,2-trichloroethane		(a,b)
trichloroethene	trichloroethylene	(a,b)
trichloromethanethiol		(a)
trichloromonofluoromethane	trichlorofluoromethane	(a,b)
1,2,3-trichloropropane		(a)
trichlorotrifluoroethane		(b)
vinyl acetate		(a)
vinyl chloride		(a,b)

(a) ITD listed volatile organic compound.
(b) DSS listed volatile organic compound (Tables 2-2 and/or 4-1).

TABLE III-15
ITD AND/OR DSS LISTED VOLATILE ORGANIC COMPOUNDS
IDENTIFIED IN PATENTS AS POTENTIALLY USED IN
PHARMACEUTICAL PRODUCT MANUFACTURE

Compound	Subcategory Usage A	B	C
Priority Pollutants			
acrylonitrile			X
benzene	X	X	X
bromomethane			X
chlorobenzene	X		X
chloroform	X	X	X
chloromethane	X		X
ethylene diehloride			X
methylene chloride	X	X	X
tetrachloromethane	X	X	X
toluene	X	X	X
trichloroethylene		X	X
Non-Priority Pollutants			
acetaldehyde			X
acetonitrile	X	X	X
acetophenone	X		X
acetyl chloride	X	X	X
aniline	X		X
2-butanone (MEK)	X		X
n-butyl alcohol	X	X	X
carbon disulfide			X
cyclohexane	X		X
diethylamine			X
dimethylamine			X
n,n-dimethylformamide	X		X
dimethyl sulfoxide	X	X	X
1,4-dioxane	X	X	X
ethanol, 2-chloro			X
ethyl acetate	X	X	X
ethylene oxide	X		X
ethyl ether	X	X	X
formaldehyde	X	X	X
formic acid	X	X	X
furfural	X		
hydrazine			X
iodomethane	X		X
isobutyl alcohol		X	X
methanol	X	X	X
methyl mercaptan			X
methyl methacrylate			X
4-methyl-2-pentanone (MIBK)	X		X
2-propanone (acetone)	X	X	X
pyridine	X	X	X
tetrahydrofuran	X		X
total xylenes	X	X	X
vinyl acetate			X

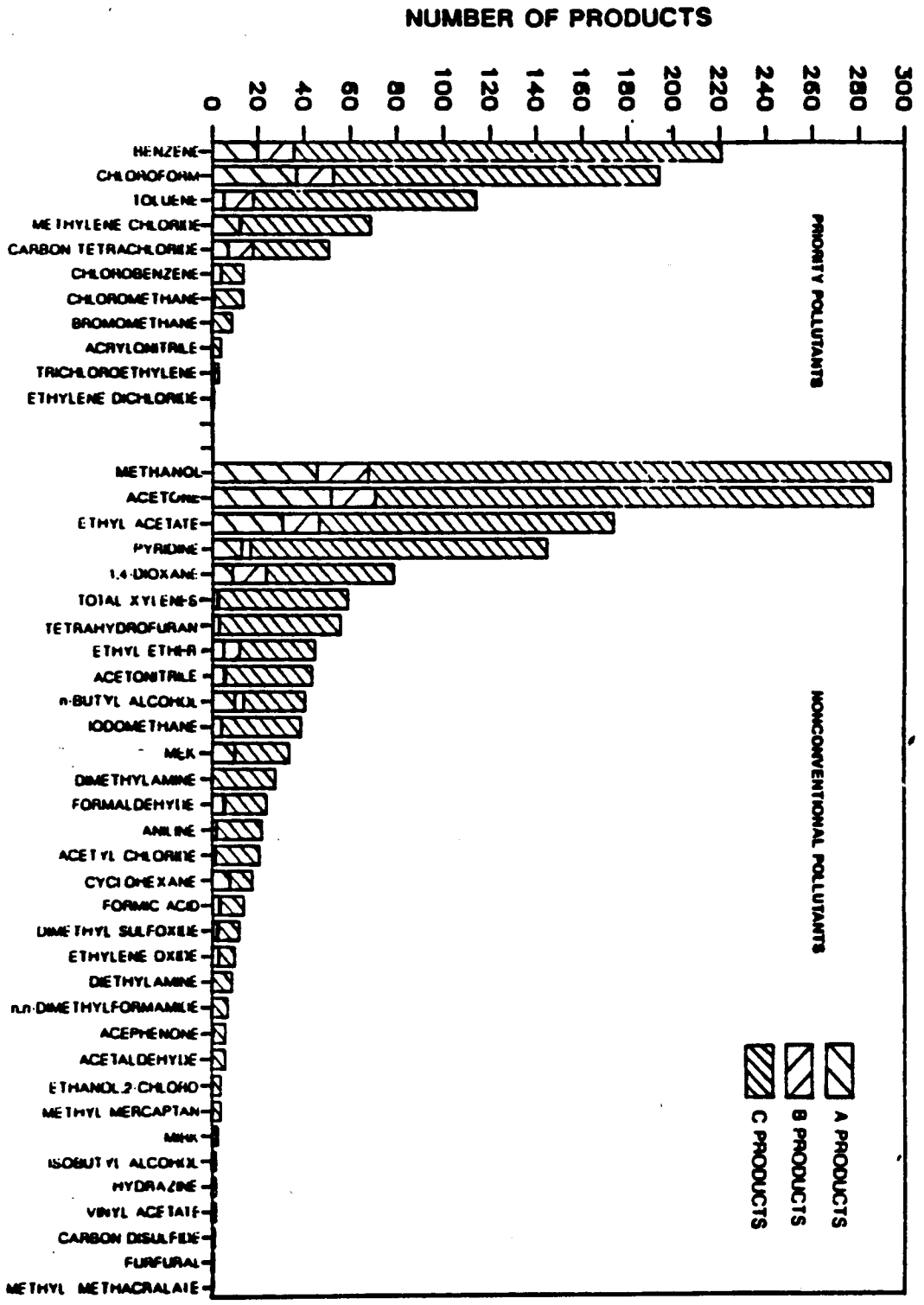


FIGURE III-2

VOLATILE ORGANIC COMPOUNDS POTENTIALLY USED IN SUBCATEGORY A,B,and C PRODUCT MANUFACTURE

BASED ON PRODUCT PATENT REVIEW

TABLE III-16

NUMBER OF PHARMACEUTICAL PRODUCTS THAT MAY USE
THE FOLLOWING PRIORITY POLLUTANTS IN THEIR MANUFACTURE

Plant/Subcategory		Priority Pollutant Compounds										
		acrylo-nitrile	benzene	bromo-methane	chloro-benzene	chloroform	chloro-methane	ethylene dichloride	methylene chloride	carbon tetrachloride	toluene	trichloro-ethylene
Direct Dischargers												
11111	C		3		1	2					1	
12022	A,C		6		(0)	(9)	(0)	(0)	(4)		(1)	
12026	C		2							1	1	
12036	A,D		(0)			1					(0)	
12038	A,B,C,D		6			6			1	3	2	
12097**	C,D		8			4	1		3	2	3	
12132	A,C	(0)*	(3)			(3)	1		(2)	3	(2)	(0)
12161	A,C,D		(1)*			(1)			1	1*	(0)	
12187	C		3		(0)*	1					(1)*	
12236	C		(2)		1				0*	0*	(0)*	
12256	A,B,C,D		(9)[1]	2		(8)	(1)		(1)		(5)	
12407	C	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
12462	A					1		1				1
12471	B										(0)[4]	
20245	A,C	(0)	(0)*		0*	1*		1	0*		(0)*	1*
20246	C		2		1	1	1		1	1	1	
20257	C		(0)								(0)	
20297	C		(1)			1			1		(0)	
33333	C	1	1			1						
Number of Direct Discharge Users												
Patent Data		1	13	1	3	14	4	2	8	6	9	2
306 Data		4	10	1	3	6	3	2	5	1	12	2
Indirect Dischargers												
12003	A,C,D		(16)	(1)	(3)	(8)*	(1)	(0)	(5)*	2	(5)*	
12004	C,D		1			1					1	
12005	B					(0)[2]				(0)[2]		
12012	B					(0)						
12016	A,C,D					(2)						
12037	C,D		(0)						(0)*			
12040	B,D		1			1						
12042**	A,B,D		2		1	1				1	2	
12043**	C		1									
12044	A,D		(0)			(0)			(0)		(0)	
12048	C,D		(1)			(1)						
12052	C,D							(0)				
12057	C,D		(2)					(0)	(0)	(0)	(0)	
12062	C,D					(0)			(0)			
12066	B,C,D		1			1			1	1	1	
12077	C,D		(2)	(0)		(1)					(1)	
12084	B,C,D		(5)			(5)		(0)	(0)		(7)	
12087	C		4		(1)	(3)		(0)	(0)		(1)	

TABLE III-16 (continued)

NUMBER OF PHARMACEUTICAL PRODUCTS THAT MAY USE
THE FOLLOWING PRIORITY POLLUTANTS IN THEIR MANUFACTURE

Plant/Subcategory		Priority Pollutant Compounds										
		acrylo-nitrile	benzene	bromo-methane	chloro-benzene	chloroform	chloro-methane	ethylene dichloride	methylene chloride	carbon tetrachloride	toluene	trichloro-ethylene
12100	C,D					(0)			(0)			
12102	C,D		(3)		(0)	1					(0)	
12108**	A,C,D		1			1			2	1		
12111	B,D					(0)				(0)		
12123	C,D	1	(6)*		0*	(5)*		(0)*	(0)*	0*	(6)*	
12135	B,C,D		(11)*		0*	(5)*	(1)	0*	(2)*	2	(2)*	0*
12155	C,D		(0)[1]			2			(0)		(0)	
12168	A,B,C,D		(3)	(0)		(4)	1			(0)	(2)*	
12199	A,C,D		1			(2)	2					
12204**	A,B,C,D		0*			4*			0*		1*	1
12226	B					(0)[3]						
12230	B					2			2		1	
12231	A,D		1			1			(0)			
12235	C										(0)	
12240	C,D		1			1						
12244	C		(0)			(0)			(0)		(0)	
12245	A,B,C,		4			2				1	(2)*	
12246	C,D					(0)		(0)	(0)	(0)	(0)	
12247	C										(0)[4]	
12252	A,C,D		(6)			(4)*	(0)		(0)*	(0)	(4)*	
12254	A,D					(1)*			(0)		(0)	
12257	A,B,C,D	0*	(8)	(0)		(5)*	(1)	(0)	(2)*	(1)	(2)*	(0)
12264	A,B,D		(1)			(1)			(0)	(0)	1	(0)
12265	B,D					(0)			(0)			
12275	B,C		(7)		(0)*	(4)*		(0)*	(0)	1	(5)*	
12294	C,D	1	6			6	1		(1)*	1	1	
12302	C									(0)*		
12310	C,D	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	
12311	A,B,C,D		(1)			2		1	(2)	1	(2)	
12312	B,D		(0)	(0)		(1)	(0)	(0)	(0)		(0)	
12330	A,B,C,D		(2)			(2)			(1)*	(0)	(1)	(0)
12332	C		1			(1)					1	(0)
12333	C,D				(0)	(0)			(0)		(0)	
12339	A,C,D		(2)[1]			2*			(1)*	2*	(0)[1]	
12342	A,C,D		4			11			(7)*	2	4*	
12343	A,C,D		1			(3)			(3)		(1)	
12411	B,C,D	(1)	6			(2)*	(0)		(1)*		(0)*	
12419	B,D										(0)	
12420	B,D		3			3		(0)		3	(3)	
12439	C,D		(0)									
12447**	A,B,C,D		23			29	4	0*	16*	6	17*	(0)
12472	B,C		2			2			1		1	1
12473	B,C					(0)			(0)	(0)	(0)	
12477	B,C		(3)			(1)			(0)*	(1)	(1)	(0)
20012	C		1								(0)	

TABLE III-16 (continued)

NUMBER OF PHARMACEUTICAL PRODUCTS THAT MAY USE
THE FOLLOWING PRIORITY POLLUTANTS IN THEIR MANUFACTURE

Plant/Subcategory		Priority Pollutant Compounds: acrylonitrile	benzene	bromomethane	chlorobenzene	chloroform	chloromethane	ethylene dichloride	methylene chloride	carbon tetrachloride	toluene	trichloroethylene
20139	C,D		6		3	4	1				(1)	
20177	C					1					(1)	
20203	C		1	(0)			(0)		(0)	(0)	(1)	
20205**	C,D		1				0		0		1	
20234	C		2							1	2	
20254	C					1					(0)	
20310	C		2			(0)			(0)		(2)	
20311**	C		1			2			1		1	
20312	B,C,D							(0)				
20331	C		9	(0)	1	1	(0)		(0)		(5)	
20349	C									1	(2)	
20350	C,D							(0)[1]				
20473	B									(0)[5]		
Number of Indirect Discharge Users												
Patent		3	44	1	5	45	8	1	16	17	36	1
308		2	27	8	6	38	10	13	41	14	46	6

[1] No longer used
[2] 308 Information indicates usage is less than 50 mℓ/yr.
[3] 308 Information indicates usage in 120 gallons per year.
[4] 308 Information indicates minor usage.
[5] 308 Information indicates usage is 1.5 gallons per week.

( ) Parentheses indicate that the compounds used in manufacturing operations based on 308 portfolio information.
* Indicates that the compound has been detected in the plants wastewater.
** 308 portfolio information for this plant is confidential.

- The patent search method was very accurate in indicating which priority pollutant solvents are commonly used (i.e., benzene, chloroform, methylene chloride, and toluene).

- The patent search method was relatively accurate in determining which plants were likely to be using the more common priority pollutant solvents; with the accuracy of the method increasing as the number of products potentially using a given solvent increases.

- The patent search method showed poor accuracy in identifying plants using the less common solvents (e.g, bromomethane, ethylene dichloride, and trichloroethylene).

It is expected that these observations would be true for the hazardous nonconventional pollutant solvents as well.

2. Sampling and Analysis Programs

Since 1985, EPA has conducted sampling episodes at six pharmaceutical manufacturing facilities, providing information that characterizes industry wastes with respect to hazardous constituents beyond those on the priority pollutant list. The first episode was conducted at Plant 12135. This sampling effort was conducted concurrent with, and in support of, preparation of the DSS. At this facility, a single raw wastewater sample was collected and analyzed for conventional pollutants (excluding fecal coliform), priority pollutants (excluding asbestos), and approximately 250 additional organic and inorganic parameters. A complete list of parameters analyzed for at Plant 12135 is presented in Appendix G.

Four additional pharmaceutical manufacturing facilities (Plants 12204, 12236, 12247, and 99999) were sampled in 1986 and 1987 to provide data for this document. The four plants chosen were selected from a field of candidates producing pharmaceutical products by fermentation and/or chemical synthesis processes

(Subcategories A and/or C). Based on information available to EPA (e.g., literature, previous sampling episodes, patent review), Subcategory A and C facilities have the greatest potential for discharging significant quantities of priority and hazardous nonconventional pollutant solvents. Subcategory B and D facilities were excluded because they generally produce low volume, low strength wastewater, resulting in low potential for discharging significant quantities of the pollutants of concern. The field of candidates included 96 indirect dischargers and 26 direct dischargers.

Even though the primary objective of this sampling was to obtain additional information on the discharge of hazardous constituents to POTWs, EPA intentionally chose one direct discharger to evaluate

the presence, treatability, and fate of the pollutants of concern at direct discharging pharmaceutical manufacturing facilities. Raw wastewater samples were collected at all four plants. Treated effluents and sludges were also collected whenever possible. With a few minor exceptions, all samples were analyzed for pollutants on the 1987 ITD List of Analytes. The list includes conventional pollutants (excluding fecal coliform) and 285 other organic and inorganic parameters (see Appendix D). Methods used to analyze the wastewater and sludge sampled for the ITD List of Analytes are listed in Appendix H.

Between January and June 1987, limited sampling was done at a sixth pharmaceutical facility (Plant 88888). This plant was participating in a pilot program, with EPA evaluating the ability of ACA technologies to reduce COD levels. The raw wastewater at this facility was sampled on ten occasions and was analyzed for a limited number of constituents that are on the ITD List of Analytes. Results of all six sampling episodes are presented in the following paragraphs.

a. Plant 12135. This plant is a large pharmaceutical manufacturing facility producing products by extraction, chemical synthesis, and formulation operations (Subcategories B, C, and D, respectively). It generates approximately 1.0 mgd of process wastewater that is discharged to a POTW. This facility also discharges sanitary and some additional wastewater (normally from research operations) to a separate POTW.

Wastewater treatment at this facility consists of equalization followed by pH adjustment. The neutralized wastewater is sent to the local POTW. A single 24-hour composite sample of the neutralized process wastewater was collected. A schematic of the wastewater treatment system showing the sampling point is shown in Figure III-3.

Analytical results of the sample collected are summarized in Table III-17. Only the analytical parameters yielding a detected value are reported.

b. Plant 12204. This plant is a large pharmaceutical manufacturing facility producing products by fermentation, extraction, chemical synthesis, and mixing/compounding/formulating operations (Subcategories A, B, C, and D, respectively). It generates approximately 0.8 mgd of process wastewater that is pretreated prior to discharge to the local POTW. The principal sources of wastewater are the fermentation and chemical synthesis operations. Wastewater treatment at this facility consists of pH adjustment with lime, followed by primary clarification, followed by oxygen-activated sludge treatment. Waste sludge from the primary and secondary clarifiers is dewatered separately on belt

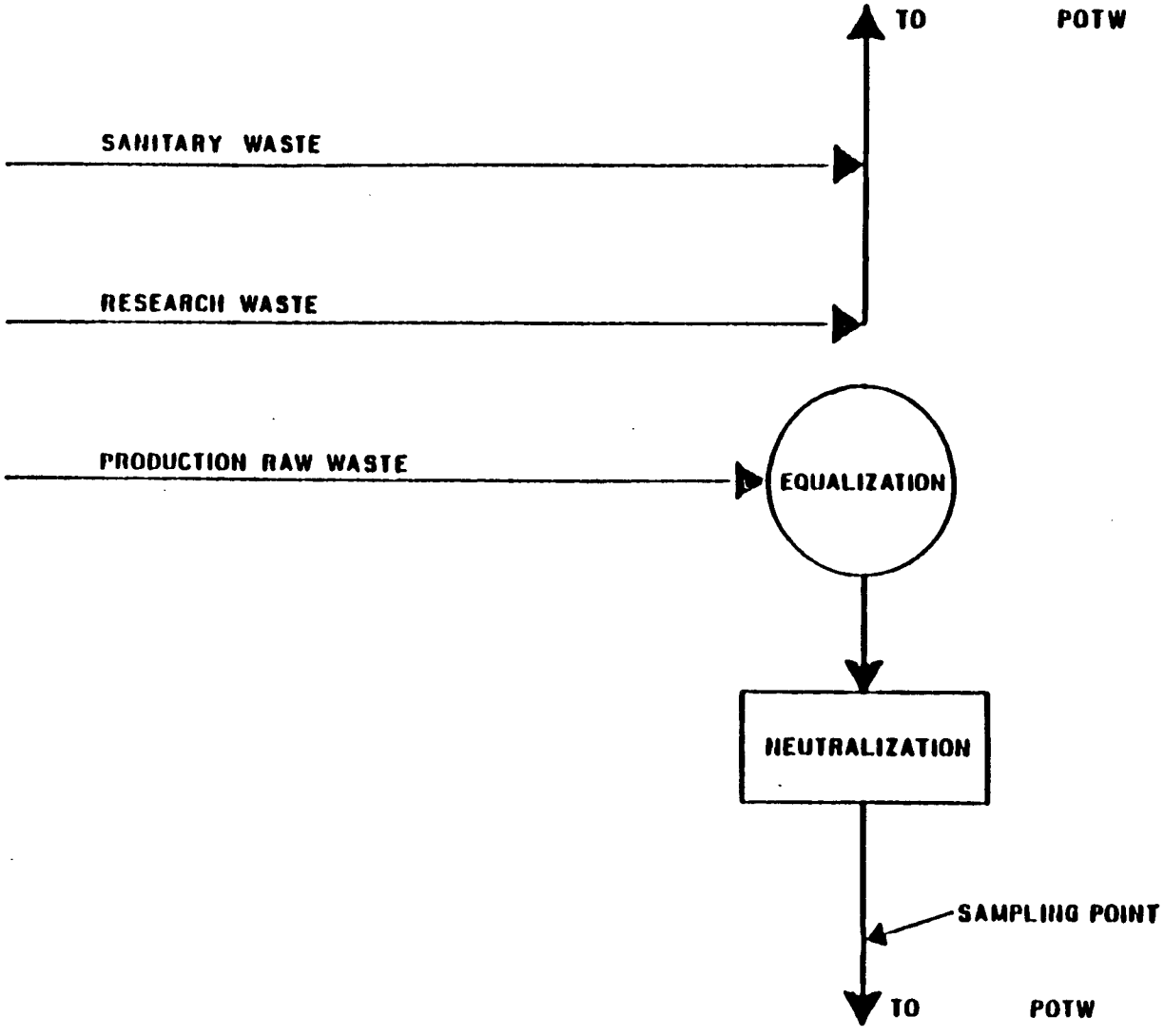


FIGURE III-3
PLANT NO. 12135
WASTEWATER PRETREATMENT SYSTEM

TABLE III-17

SUMMARY OF REPORTED ANALYTICAL RESULTS
PLANT 12135

Pollutant Category and Pollutant	Raw Waste (µg/ℓ)
Volatile Organics	
benzene*	17
chlorobenzene*	19
chloroform*	50
1,1-dichloroethane*	76
1,2-dichloroethane*	2,497
1,1-dichloroethene*	22
trans-1,2-dichloroethene*	442
ethylbenzene*	136
methylene chloride*	2,760
tetrachloroethene*	43
1,1,1-trichloroethane*	393
trichloroethene*	87
toluene*	1,565
vinyl chloride*	42
acetone	4,592
2-butanone (MEK)	1,566
diethylether	287
Semivolatile Organics	
1,2-dichlorobenzene*	2,280
Pesticides/Herbicides	
BHC, Beta*	1.198
BHC, Delta*	0.012
4,4'-DDD*	0.914
endrin ketone	1.20
Dioxins/Furans	
2,3,7,8-TCDD*	--

TABLE III-17 (continued)

Pollutant Category and Pollutant	Raw Waste (µg/ℓ)
Metals	
antimony*	15
arsenic*	8
cadmium*	8
chromium*	99
copper*	45
iron	2,140
lead*	13
lithium	1,140
mercury*	0.4
strontium	410
zinc*	303
Classical Pollutants	
ammonia, as N (mg/ℓ)	561
BOD5, carbonaceous (mg/ℓ)	1,900
chemical oxygen demand (mg/ℓ)	4,350
cyanide, total*	<0.02
fluoride mg/ℓ	0.8
nitrate + nitrite, as N (mg/ℓ)	<0.02
total organic carbon (mg/ℓ)	300
total suspended solids (mg/ℓ)	64
Field Measurements	
temperature, water (°C)	23-29
pH	6.5-8.0

* Priority Pollutants

filter presses. The dewatered sludges are combined and mixed with fermentation wastes and leaves, then composted on-site. The composted sludge is sold as a soil conditioner. Approximately 10 to 12 dry tons of waste sludge are generated daily.

Two consecutive, separate, and complete 24-hour samples were taken of the raw waste and treated effluent. Single grab samples were collected of tap water, thickened primary sludge, dewatered primary sludge, and dewatered secondary sludge. A schematic of the wastewater treatment system showing sample point locations is shown in Figure III-4. Analytical results of the samples collected are presented in Table III-18. Only the analytical parameters yielding an analytically detectable value are reported.

c. Plant 12236. This plant manufactures pharmaceutical products by chemical synthesis processes (Subcategory C). Approximately 1.8 mgd of wastewater is treated in this wastewater treatment system prior to being discharged to a river. The wastewater sources at this facility are process wastewater, air pollution control scrubber wastewater, wastewater from cyanide destruct units, pretreated sanitary wastewater, and some adsorption tower wastewater. Noncontact cooling water is not treated in the wastewater treatment facility prior to discharge.

Wastewater treatment at this facility consists of flow equalization, followed by pH adjustment with lime or caustic, followed by primary clarification, followed by conventional air-activated sludge treatment. Primary and waste-activated sludges are thickened in a gravity thickener, dewatered on a belt filter press, and disposed of in a RCRA-licensed landfill. Approximately 5 dry tons of sludge are disposed of daily.

Two consecutive, separate, and complete 24-hour wastewater samples were taken of raw waste and treated effluent. Single grab samples of tap water, thickened sludge, and dewatered sludge were collected. A schematic of the wastewater treatment system showing sample point locations is shown in Figure III-5.

Analytical results of the samples collected are in Table III-19. Only the analytical parameters yielding an analytically detectable value are reported.

d. Plant 12447. This plant is a large pharmaceutical manufacturing facility (Subcategories A, B, C, and D) producing ethical drugs, particularly antibiotics, antidiabetics, steroids, and a variety of nutritional, veterinary, and agricultural products. Approximately 2.0 mgd of process wastewater is generated primarily from fermentation operations and the production of fine chemicals. Wastewater is not pretreated before discharge to the local POTW. Due to health and safety concerns about obtaining combined raw waste samples in the lower level of the sampling station, sampling was limited to large grab samples. The first grab

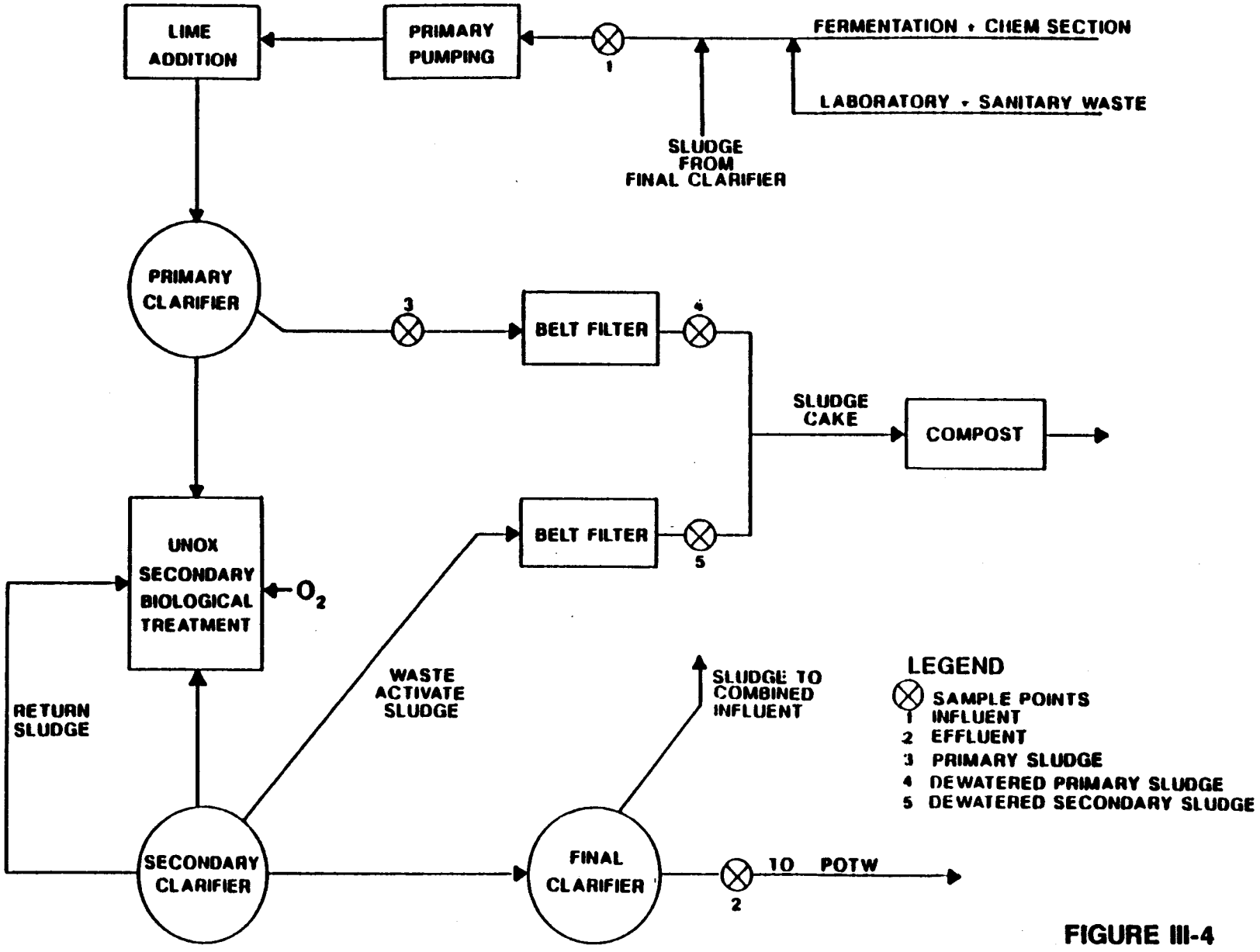


FIGURE III-4
PLANT NO. 12204
WASTEWATER PRETREATMENT SYSTEM

TABLE III-18
ITD/RCRA SAMPLING PROGRAM
SUMMARY OF REPORTED ANALYTICAL RESULTS
PLANT 12204

Pollutant Category and Pollutant	Tap Water (µg/ℓ)	Wastewater Day 1 Raw Waste (µg/ℓ)	Wastewater Day 1 Treated Effluent (µg/ℓ)	Wastewater Day 2 Raw Waste (µg/ℓ)	Wastewater Day 2 Treated Effluent (µg/ℓ)	Primary Sludge Thickened Primary (mg/kg)	Primary Sludge Dewatered Primary (mg/kg)	Primary Sludge TCLP Extract (µg/ℓ)	Secondary Sludge Dewatered Secondary (mg/kg)	Secondary Sludge TCLP Extract (µg/ℓ)
Volatile Organics										
acrolein*	--	75	--	--	--	--	--	--	--	102
benzene*	--	24	31	--	--	--	--	--	--	--
chloroform*	--	596	62	77	51	--	--	--	--	--
1,1-dichloroethane*	28	--	30	--	--	--	--	--	0.155	21
trans-1,2-dichloroethene*	--	--	25	--	--	0.236	--	--	0.114	25
methylene chloride*	--	4,839	5,167	4,696	--	7.109	0.929	63	--	52
toluene*	20	504	362	4,181	7,896	500	--	--	0.100	37
1,1,1-trichloroethane*	--	87	62	--	--	--	--	--	--	--
acetone	--	173,570	110,395	5,678	1,106	504.209	282.229	14,081	66.955	17,028
diethyl ether	--	16,627	14,288	--	530	--	2.368	61	--	--
isobutyl alcohol	--	--	--	--	--	--	--	--	--	140
2-butanone (MEK)	--	--	--	--	--	--	--	--	--	980
vinyl acetate	--	99	63	--	--	--	--	--	--	--
Semivolatile Organics										
phenol	--	--	--	--	124	19.655	2.079	15	--	--
Dioxins/Furans										
Not Analyzed										

TABLE III-18 (continued)

Pollutant Category and Pollutant	Tap Water (µg/ℓ)	Wastewater Day 1 Raw Waste (µg/ℓ)	Wastewater Day 1 Treated Effluent (µg/ℓ)	Wastewater Day 2 Raw Waste (µg/ℓ)	Wastewater Day 2 Treated Effluent (µg/ℓ)	Primary Sludge Thickened Primary (mg/kg)	Primary Sludge Dewatered Primary (mg/kg)	Primary Sludge TCLP Extract (µg/ℓ)	Secondary Sludge Dewatered Secondary (mg/kg)	Secondary Sludge TCLP Extract (µg/ℓ)
Metals										
beryllium*	--	--	--	--	--	--	1	--	0.5	--
cadmium*	--	--	--	5	--	--	--	--	2	--
chromium*	--	12R	--	16	--	2	5	--	6	--
copper*	--	165	71	160	30	20	41	219	44	--
lead*	--	--R	--	--	--	--	--	--	16	--
mercury*	--	--	--	--	--	0.9	0.3	0.4	0.9	--
nickel*	--	--	--	--	--	2	5	--	10	--
selenium*	--	12s+	10	--	s+	--	--	--	--	--
silver*	--	--	--	--	--	0.6	1.8	--	1.8	--
zinc*	143	303R	181	284	124	31	73	212	3	722
aluminum	--	2,250	1,740	2,730	799	205	1,900	581	1,610	270
barium	52	124	88	130	79	7	24	591	21	1,090
boron	--	--R	--	--	--	--	--	377	--	668
calcium	28,900	240,000	274,000	309,000	231,000	881	198,000	2,660,000	167,000	369,000
iron	91	2,110R++	1,020	3,150	721	288	850	--	753	521
magnesium	8,950	32,800R	22,000	39,400	23,400	377	1,040	--	923	5,860
manganese	--	376R	182	574	205	18	40	--	38	357
sodium	35,000	370,000R	238,000	273,000	264,000	435	413	6,700	653	1,380,000
tin	--	--R	--	--	--	5	10	--	7	--
titanium	--	--R	--	--	--	7	61	--	24	--
vanadium	--	--	--	--	--	3	8	--	3	--
Elements										
iodine	--	19,000e	5,000e	24,000e	--	36e	--	NA	26e	NA
neodymium	--	--	--	--	--	--	--	NA	37e	NA
phosphorus	1,000e	24,000e	9,000e	29,000e	7,000e	1,180	0.5e	NA	2,000e	NA
potassium	--	1,000e	1,000e	2,000e	1,000e	--	--	NA	--	NA
silicon	4,000e	10,000e	10,000e	10,000e	9,000e	29e	--	NA	376e	NA
strontium	100e	200e	300e	400e	200e	6e	0.4e	NA	62e	NA
sulfur	7,000e	434,000e	207,000e	260,000e	243,000e	667e	12e	NA	2,200e	NA

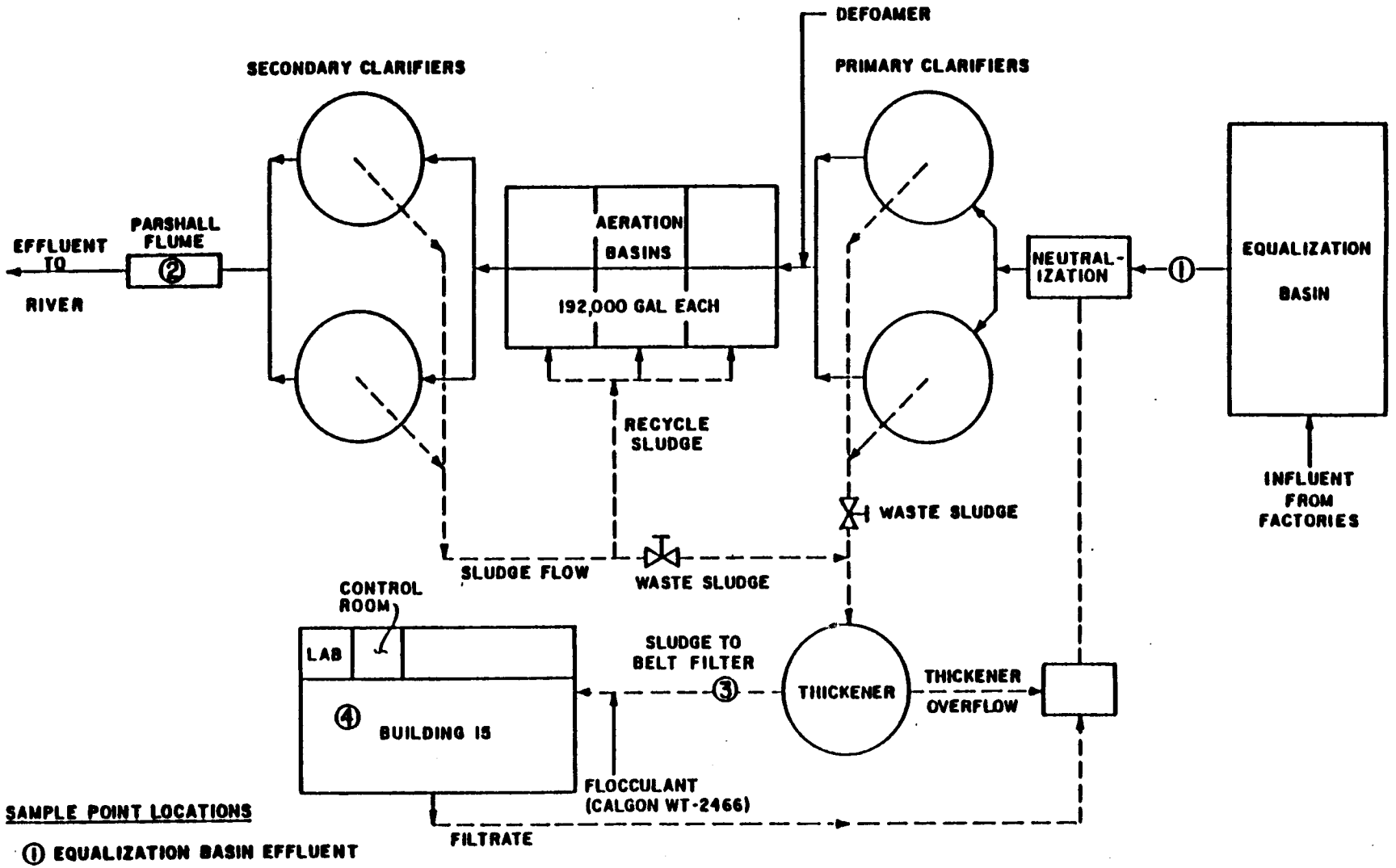
TABLE III-18 (continued)

Pollutant Category and Pollutant	Tap Water (µg/ℓ)	Wastewater Day 1 Raw Waste (mg/ℓ)	Wastewater Day 1 Treated Effluent (mg/ℓ)	Wastewater Day 2 Raw Waste (mg/ℓ)	Wastewater Day 2 Treated Effluent (mg/ℓ)	Primary Sludge Thickened Primary (mg/kg)	Primary Sludge Dewatered Primary (mg/kg)	Primary Sludge TCLP Extract (µg/ℓ)	Secondary Sludge Dewatered Secondary (mg/kg)	Secondary Sludge TCLP Extract (µg/ℓ)
Classical Pollutants										
ammonia, as N	NA	NR	NR	NR	78	4,600	940	NA	4,600	NA
BOD5 Day (carbonaceous)	NA	1,300	350	2,100**	380**	NA	NA	NA	NA	NA
chemical oxygen demand	NA	4,100	800	3,600	800	NA	NA	NA	NA	NA
cyanide, total*	NA	--	--	--	--	--	4.5	NA	--	NA
fluoride	NA	0.32	0.32	0.24	0.24	NA	NA	NA	NA	NA
nitrate-nitrite, as N	NA	0.50	0.061	1.9**	0.12**	1.1	--	NA	3.4	NA
nitrogen, kjeldahl, total	NA	NR	NR	NR	190	4,300	14,000	NA	7,000	NA
oil and grease, total recoverable	NA	86c	36c	89c	14c	NA	NA	NA	NA	NA
residue, filterable	NA	2,700	1,500	2,400**	1,900**	NA	NA	NA	NA	NA
residue, non-filterable	NA	1,400	300	1,600	220	NA	NA	NA	NA	NA
sulfide, total (iodometric)	NA	19c	9.5c	20c	5.4c	NA	NA	NA	NA	NA
total phosphorus, as P	NA	19	7	21	5.6	NA	NA	NA	NA	NA
total organic carbon	NA	1,100	210	890	220	NA	NA	NA	NA	NA
flash point (°C)	NA	NA	NA	NA	NA	NA	52	NA	37	NA
pH, soil	NA	NA	NA	NA	NA	7.6	12.8	NA	7.5	NA
residue, total (%)	NA	NA	NA	NA	NA	11	38	NA	22	NA
residue, total volatile (%)	NA	NA	NA	NA	NA	46	7.4	NA	53	NA
sulfide, total (Monier-Williams)	NA	NA	NA	NA	NA	640	88	NA	75	NA
corrosivity (mpy)	NA	NA	NA	NA	NA	NA	<10	NA	<10	NA

TABLE III-18 (continued)

Pollutant Category and Pollutant	Tap Water	Wastewater Day 1 Raw Waste	Wastewater Day 1 Treated Effluent	Wastewater Day 2 Raw Waste	Wastewater Day 2 Treated Effluent	Primary Sludge Thickened Primary	Primary Sludge Dewatered Primary	Primary Sludge TCLP Extract	Secondary Sludge Dewatered Secondary	Secondary Sludge TCLP Extract
Field Measurements										
process flow (mgd)	NA	2.12	2.12	1.93	1.93	NA	NA	NA	NA	NA
pH	NA	5.9-10.8	7.4-9.1	6.0-10.7	7.0-8.5	NA	NA	NA	NA	NA
settleable solids (mg/ℓ)	NA	94	18	100	75	NA	NA	NA	NA	NA
temperature, water (°C)	NA	20-26	18-26	20-30	22-26	NA	NA	NA	NA	NA

\+ Indicates the correlation coefficient for Method of Standard Addition.
++ Indicates duplicate analysis is not within control limits.
-- Indicates pollutant concentration below detection limit.
NA Indicates not analyzed.
c Average of grab sample results.
e Indicates an estimated value.
t Denotes tentative identification below the detection limit.
DET Indicates pollutant concentration qualitatively detected.
NR No value reported due to matrix interference.
* Priority pollutant.
** Analysis performed after expiration of analytical hold-time. Refer to report of analysis, for further information.
R Indicates spike recovery is not within control limits.
S Indicates the correlation coefficient for Method of Standard addition is less than 0.995.



SAMPLE POINT LOCATIONS

① EQUALIZATION BASIN EFFLUENT

② FINAL EFFLUENT

③ THICKENED SLUDGE

④ DEWATERED SLUDGE

FIGURE III-5
PLANT NO. 12236
WASTEWATER TREATMENT SYSTEM

TABLE III-19
ITD/RCRA SAMPLING PROGRAM
SUMMARY OF REPORTED ANALYTICAL RESULTS
PLANT 12236

Pollutant Category and Pollutant	Tap Water (µg/ℓ)	Wastewater-Day 1 Raw Waste (µg/ℓ)	Wastewater-Day 1 Treated Effluent (µg/ℓ)	Wastewater-Day 2 Raw Waste (µg/ℓ)	Wastewater-Day 2 Treated Effluent (µg/ℓ)	Combined Sludge Thickened Sludge (mg/kg)	Combined Sludge Dewatered Sludge (mg/kg)	Combined Sludge TCLP Extract (µg/ℓ)
Volatile Organics								
carbon tetrachloride*	--	--	42	--	--	--	--	--
1,1-dichloroethane*	--	--	--	--	--	--	0.045	20
methylene chloride*	--	114	158	10,745	21	--	--	--
toluene*	31	--	19	--	--	--	0.077	140
acetone	--	1,795	96	--	174	--	0.555	--
2-hexanone	--	--	1,087	--	--	--	--	--
methacrylonitrile	--	--	--	--	--	--	0.191	106
Semivolatile Organics								
bis(2-chloroethyl)ether*	--	--	--	--	--	--	3.350	--
n-octadecane	--	--	--	--	--	--	2.036	--
Metals								
antimony*	--	--	--	--	--	53	6	--
cadmium*	--	--	--	--	--	--	17	15
chromium*	--	18	22	26	--	10	10	--
copper*	51	--	--	--	--	--	26	--
mercury*	--	--	--	--	--	2.5	1.6	--
nickel*	--	--	--	41	--	--	19	85
silver*	--	--	--	--	--	--	2	--
zinc*	--	117	20	164	50	88	135	1,310

TABLE III-19 (continued)

Pollutant Category and Pollutant	Tap Water (µg/ℓ)	Wastewater-Day 1 Raw Waste (µg/ℓ)	Wastewater-Day 1 Treated Effluent (µg/ℓ)	Wastewater-Day 2 Raw Waste (µg/ℓ)	Wastewater-Day 2 Treated Effluent (µg/ℓ)	Combined Sludge Thickened Sludge (mg/kg)	Combined Sludge Dewatered Sludge (mg/kg)	Combined Sludge TCLP Extract (µg/ℓ)
Metals (continued)								
aluminum	113	118	--	178	--	102	253	500
barium	--	--	--	218	--	37	44	1,370
boron	--	209	--	--	--	--	89	1,050
calcium	10,400	51,700	63,700	51,500	51,200	8,340	12,000	64,700
cobalt	--	--	--	--	--	--	18	--
iron	60	121,000	4,130	171,000	5,710	92,900	18,800	119,000
magnesium	1,590	1,680	1,440	1,810	1,340	726	1,170	3,840
manganese	--	794	255	1,380	222	365	665	1,940
osmium	--	--	200e	100e	300e	--	--	NA
sodium	5,420	1,530,000	1,410,000	1,720,000	1,650,000	23,500	5,760	1,430,000
tin	--	--	--	--	--	60	16	--
titanium	--	85	--	126	--	72	107	--
vanadium	--	86	--	129	--	77	120	--
Elements								
iodine	--	31,000e	1,000e	39,000e	10,000e	39e	221e	NA
lanthanum	--	--	--	--	--	--	3e	NA
lutetium	--	--	--	--	--	--	6e	NA
phosphorus	--	40,000e	6,000e	48,000e	17,000e	48e	7,260e	NA
ruthenium	--	--	--	--	--	--	87e	NA
silicon	4,000e	3,000e	3,000e	3,000e	3,000e	0.5e	26e	NA
strontium	--	100e	100e	100e	--	--	6e	NA
sulfur	5,000e	614,000e	559,000e	596,000e	605,000e	29e	3,130e	NA
thorium	--	--	--	--	--	--	29e	NA
uranium	--	--	--	--	--	--	58e	NA
zirconium	--	--	--	--	--	--	3e	NA

TABLE III-19 (continued)

Pollutant Category and Pollutant	Tap Water (mg/ℓ)	Wastewater-Day 1 Raw Waste (mg/ℓ)	Wastewater-Day 1 Treated Effluent (mg/ℓ)	Wastewater-Day 2 Raw Waste (mg/ℓ)	Wastewater-Day 2 Treated Effluent (mg/ℓ)	Combined Sludge Thickened Sludge (mg/kg)	Combined Sludge Dewatered Sludge (mg/kg)	TCLP Extract (µg/ℓ)
Classical Pollutants								
ammonia, as N	NA	170	120	220	130	9,300	5,000	NA
BOD5 Day (carbonaceous)	NA	2,300	20	1,300	24	NA	NA	NA
chemical oxygen demand	NA	2,200	380	2,300	400	NA	NA	NA
cyanide, total*	NA	NR	0.025	NR	0.029	5.0	6.9	NA
nitrogen, kjeldahl, total	NA	240	140	140	140	28,000**	73,000	NA
nitrate-nitrite, as N	NA	0.26	3.9	0.23	4.0	4.5	1.1	NA
oil and grease, total recoverable	NA	--	11c	13c	26c	NA	NA	NA
residue, filterable	NA	4,800	4,100	5,200	4,400	NA	NA	NA
residue, non-filterable	NA	340	59	530	66	NA	NA	NA
total phosphorus, as P	NA	1.0	4.9	1.5	12	NA	NA	NA
total organic carbon	NA	960	72	930	79	NA	NA	NA
sulfide, total (iodometric)	NA	3.2c	--	80c	--	NA	NA	NA
corrosivity (MPY)	NA	NA	NA	NA	NA	<10	<10	NA
flash point (°C)	NA	NA	NA	NA	NA	40	35	NA
pH, soil (s.u.)	NA	NA	NA	NA	NA	8.0	7.3	NA
residue, total (%)	NA	NA	NA	NA	NA	3.9	22	NA
residue, total volatile (%)	NA	NA	NA	NA	NA	58	63	NA
sulfide, total (Monier-Williams)	NA	NA	NA	NA	NA	7,000	6,000	NA

TABLE III-19 (continued)

Pollutant Category and Pollutant	Tap Water	Wastewater-Day 1 Raw Waste	Wastewater-Day 1 Treated Effluent	Wastewater-Day 2 Raw Waste	Wastewater-Day 2 Treated Effluent	Combined Sludge Thickened Sludge	Combined Sludge Dewatered Sludge	Combined Sludge TCLP Extract
Field Measurements								
process flow (mgd)	NA	1.96	1.96	1.83	1.83	NA	NA	NA
pH	NA	8.0-9.0	7.2-7.4	7.9-8.6	7.3-7.4	NA	NA	NA
temperature, water (°C)	NA	16-18	22	13-18	18-22	NA	NA	NA
settleable solids (mg/ℓ)	NA	0.2	Trace	11	Trace	NA	NA	NA

-- Indicates pollutant concentration below detection limit.
NA Indicates not analyzed.
c Average of grab sample results.
e Indicates an estimated value.
t Denotes tentative identification below the detection limit.
* Priority pollutant.
** Mean of four replicate analysis; refer to the Laboratory Report of Analysis.
NR No value reported due to matrix interference.
DET Indicates pollutant concentration qualitatively detected.

was taken as representative of daytime operations and the second was taken as representative of nighttime operations. Analytical results from the two grab samples are presented in Table III-20. Only the analytical parameters yielding an analytically detectable value are reported.

In June of 1989, Plant 12477 officials commented to EPA that the volatile organic compound analytical results from the 1986 sampling effort (i.e., results shown in Table III-20) were not representative of their process waste water discharge to the local POTW. To address this comment, EPA requested and subsequently received volatile organic compound analytical data describing the discharge to the POTW from this plant during the last two years. POTW officials collect volatile organic samples of this facility's wastewater discharge quarterly as part of their local pretreatment program. The samples are routinely analyzed for 20 purgeable halocarbons and 5 purgeable hydrocarbons, and periodically for acetone and tetrahydrofuran. In the 1986 EPA sampling effort, EPA analyzed the plant's wastewater for all these compounds. A summary of the volatile organic compound data provided by the POTW is presented in Appendix C. The number of compounds detected, the levels at which they were detected, and the frequency at which they were detected in the POTW samples suggest that the limited 1986 sampling done by EPA did not adequately characterize this plant's volatile organic compound discharge to the local POTW.

e. Plant 99999. This plant is a large pharmaceutical manufacturing facility (Subcategories A, B, C, and D), producing antibiotics through fermentation processes, fine chemicals by reaction and synthesis, and animal feed supplements recovered from wastes of fermentation products. This plant generates approximately 0.8 mgd of process wastewater that is pretreated and discharged to the local POTW. Ninety percent of the process wastewater is generated in the fermentation and chemical synthesis areas. Of this, 75 percent is generated in fermentation operations.

Wastewater treatment at this facility consists of pH adjustment with lime or H_2SO_4, equalization, and a step-feed activated sludge system followed by degassification, and sedimentation. The equalization, aeration, and degassing tanks are covered and the off-gasses are vented to the power boilers. Waste activated sludge is dewatered in a centrifuge and disposed of by a contract hauler.

Two consecutive, separate, and complete 24-hour wastewater samples were taken of the raw waste and treated effluent. As part of the QA/QC program, duplicates of the second 24-hour sample of treated effluent were collected and analyzed. Single grab samples were collected of tap water and dewatered sludge. A schematic of the wastewater treatment system showing sample point locations is shown in Figure III-6. Analytical results of the samples collected are presented in Table II-21. Only the parameters yielding an analytically detectable value are reported.

TABLE III-20
ITD/RCRA SAMPLING PROGRAM
SUMMARY OF REPORTED ANALYTICAL RESULTS
PLANT 12447

Pollutant Category and Pollutant	Grab 1 Raw Wastewater (µg/ℓ)	Grab 2 Raw Wastewater (µg/ℓ)
Volatile Organics		
1,2-dichloroethane*	239	31
toluene*	33	398
2-butanone (MEK)	1,069	2,031
isobutyl alcohol	1,557	881
Semivolatile Organics		
bis(2-chloroethyl)ether*	11	--
2-chloronaphthalene*	183	37
2,6-dinitrotoluene*	191	--
isophorone*	84	--
2-nitrophenol*	28	--
N-nitrosodi-n-propylamine*	45	--
alpha-terpineol	--	15
benzoic acid	187	--
b-naphthylamine	68	--
hexanoic acid	11	146
n-docosane	61	--
n-eicosane	212	--
n-hexadecane	22	--
n-octacosane	29	--
o-cresol	23	--
Pesticides/Herbicides		
None Detected		
Purgeable Organic Compounds		
POC	150,000	10,000
Dioxins/Furans		
Not Analyzed		

TABLE III-20 (continued)

Pollutant Category and Pollutant	Grab 1 Raw Wastewater (µg/ℓ)	Grab 2 Raw Wastewater (µg/ℓ)
Metals		
antimony*	11	--
arsenic*	6.4	--
chromium*	17	72
copper*	100	56
nickel*	44	60
zinc*	330	220
aluminum	840	270
barium	140	110
boron	210	140
calcium	100,000	110,000
cobalt	55	26
iron	3,500	8,100
magnesium	26,000	23,000
manganese	1,100	3,200
sodium	790,000	2,800,000
titanium	36	15
Elements		
iodine	DET	DET
phosphorus	DET	DET
potassium	DET	DET
silicon	DET	DET
sulfur	DET	DET

TABLE III-20 (continued)

Pollutant Category and Pollutant	Grab 1 Raw Wastewater (mg/ℓ)	Grab 2 Raw Wastewater (mg/ℓ)
Classical Pollutants		
ammonia, as N	26	35
BOD5 Day (carbonaceous)	4,000	4,600
chemical oxygen demand	9,700	10,000
fluoride	57	29
nitrate-nitrite, as N	NR	0.08
nitrogen, Kjeldahl, total	400	330
oil and grease, total recoverable	180c	320c
residue, filterable	6,000	11,000
residue, non-filterable	2,000	2,300
sulfide, total (iodometric)	19	24
total organic carbon	2,400	2,300
total phosphorus, as P	30	29
Field Measurements		
process flow (mgd)	1.86a	1.86a

* Priority pollutant.
-- Indicates that pollutant concentration was below detection limit.
NR No value reported due to matrix interference.
(a) Average daily flow during the sampling episode.
(c) Average of grab sample results.
DET Indicates that pollutant concentration qualitatively detected.

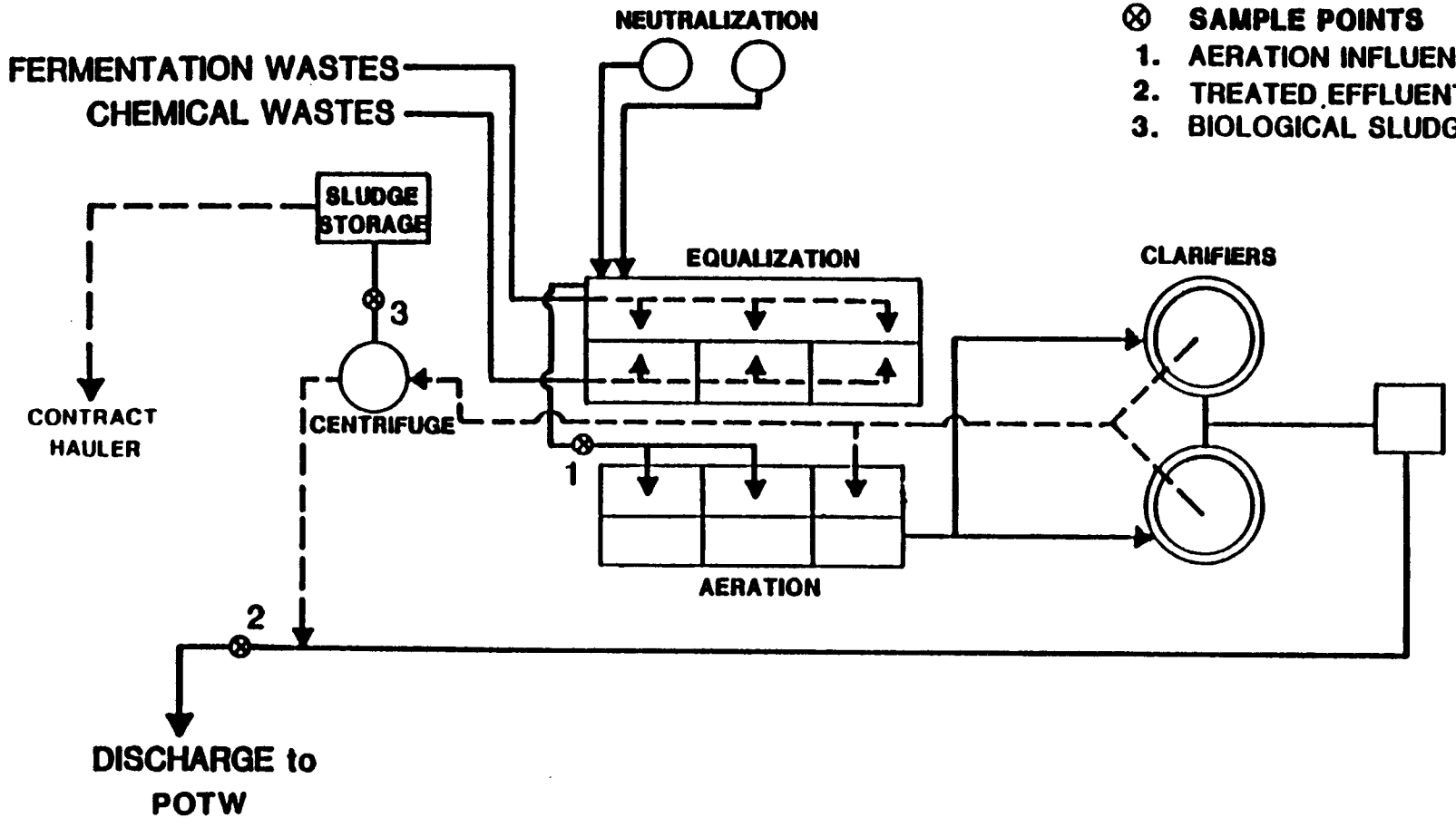


FIGURE III-6
PLANT NO.. 99999
WASTEWATER PRETREATMENT SYSTEM

TABLE III-21
ITD/RCRA SAMPLING PROGRAM
SUMMARY OF REPORTED ANALYTICAL RESULTS
PLANT 99999

Pollutant Category and Pollutant	Tap Water (µg/ℓ)	Wastewater-Day 1 Raw Waste (µg/ℓ)	Wastewater-Day 1 Treated Effluent (µg/ℓ)	Wastewater-Day 2 Raw Waste (µg/ℓ)	Wastewater-Day 2 Treated Effluent (µg/ℓ)	Wastewater-Day 2 Treated Effluent** (µg/ℓ)	Sludge Thickened Sludge (mg/kg)	Sludge TCLP Extract (µg/ℓ)
Volatile Organics								
acrylonitrile*	--	--	--	136	--	--	--	--
chloroform*	--	5,044	--	8,030	97	--	--	--
ethylbenzene*	--	659	--	--	--	--	1.145	--
methylene chloride*	--	2,086	--	14,959	176	113	--	--
toluene*	--	8,482	--	--	--	--	1.406	79
acetone	--	133,239	--	797,020	1,254	104	--	--
2-butanone (MEK)	--	742	--	--	--	--	--	--
Semivolatile Organcis								
benzidine*	--	--	224	205	192	--	--	--
bis(2-ethylhexyl) phthalate*	--	--	22	--	--	--	--	--
2-chloronaphthalene*	44	38	44	37	39	38	58.855	44
4-chloro-3-methylphenol*	--	--	--	148	--	--	--	--
3,3-dichlorobenzidine*	--	--	--	87	--	--	--	--
N-nitrosodi-n-propylamine*	--	--	--	--	82	--	--	--
alpha-terpineol	--	14	--	--	--	--	--	--
benzoic acid	--	--	--	--	--	--	--	65
diphenyl ether	--	--	--	14	--	--	--	--
2-methylnaphthalene	--	--	754	--	484	--	582.725	--
2-(methylthio)benzothiazole	--	--	--	--	--	--	--	11
n-dodecane	--	--	--	--	24	28	--	--
n-eicosane	55	--	296	206	187	142	340.855	72
n-hexacosane	--	189	--	--	--	--	--	--
n-triacontane	--	--	--	--	--	81	--	--
p-cresol	--	18	--	--	--	--	--	--

TABLE III-21 (continued)

Pollutant Category and Pollutant	Tap Water (µg/ℓ)	Wastewater-Day 1 Raw Waste (µg/ℓ)	Wastewater-Day 1 Treated Effluent (µg/ℓ)	Wastewater-Day 2 Raw Waste (µg/ℓ)	Wastewater-Day 2 Treated Effluent (µg/ℓ)	Wastewater-Day 2 Treated Effluent** (µg/ℓ)	Sludge Thickened Sludge (mg/kg)	Sludge TCLP Extract (µg/ℓ)
Pesticides/Herbicides								
BHC, alpha*	--	--	6.2	--	--	--	NA	NA
BHC, beta*	--	--	--	--	2.2	0.45	NA	NA
captan	--	--	--	--	--	0.5t	NA	NA
chloroneb	--	--	--	--	74.4t	--	NA	NA
DBCP	--	--	--	--	--	1.5t	NA	NA
etridazone	--	--	--	--	--	7t	NA	NA
trifluralin	--	17t	3.9t	--	1.9t	--	NA	NA
TEPP	--	16t	--	4,110	780	1,154	NA	NA
Purgeable Organic Compounds								
POC	100	76,000	6,800	160,000	2,700	3,100	760	NA
Dioxins/Furans								
2,3,7,8-TCDD*	NA	NA	NA	NA	NA	NA	--	NA
Metals								
arsenic*	--	18	14	16	12	7.9	--	--
chromium*	--	36	30	18	4	30	--	--
copper*	5	500	53	380	29	36	185	--
nickel*	--	66	19	33	27	23	--	--
selenium*	--	16	8.3	12	--	--	--	--
silver*	--	2.1	--	--	--	--	--	--
zinc*	91	200	38	100	26	60	79	1,200

TABLE III-21 (continued)

Pollutant Category and Pollutant	Tap Water (µg/ℓ)	Wastewater-Day 1 Raw Waste (µg/ℓ)	Wastewater-Day 1 Treated Effluent (µg/ℓ)	Wastewater-Day 2 Raw Waste (µg/ℓ)	Wastewater-Day 2 Treated Effluent (µg/ℓ)	Wastewater-Day 2 Treated Effluent** (µg/ℓ)	Sludge Thickened Sludge (mg/kg)	Sludge TCLP Extract (µg/ℓ)
Metals (continued)								
aluminum	140	3,200	1,000	2,200	630	640	3,450	558
barium	16	81	33	57	33	33	--	1,420
boron	--	97	100	77	84	75	--	704
calcium	28,000	200,000	98,000	130,000	98,000	100,000	16,000	69,400
cobalt	--	--	--	4	--	--	--	--
iron	47	2,700	720	2,000	630	690	1,050	829
magnesium	8,400	24,000	18,000	14,000	17,000	17,000	1,680	6,510
manganese	4	110	39	83	50	44	22	93
sodium	4,500	900,000	660,000	930,000	780,000	760,000	5,490	1,560,000
tin	--	--	--	--	--	--	--	109
titanium	10	57	100	59	100	100	--	--
vanadium	--	9	4	7	--	--	--	--
Elements								
germanium	--	--	--	DET	DET	--	--	NA
iodine	--	DET	DET	DET	DET	DET	DET	NA
lithium	--	--	DET	DET	DET	DET	--	NA
phosphorus	--	DET	DET	DET	DET	DET	DET	NA
potassium	--	DET	DET	DET	DET	DET	--	NA
silicon	DET	DET	DET	DET	DET	DET	--	NA
sulfur	DET	DET	DET	DET	DET	DET	DET	NA
tellurium	--	--	--	--	--	DET	--	NA

TABLE III-21 (continued)

Pollutant Category and Pollutant	Tap Water (mg/ℓ)	Wastewater-Day 1 Raw Waste (mg/ℓ)	Wastewater-Day 1 Treated Effluent (mg/ℓ)	Wastewater-Day 2 Raw Waste (mg/ℓ)	Wastewater-Day 2 Treated Effluent (mg/ℓ)	Wastewater-Day 2 Treated Effluent** (mg/ℓ)	Sludge Thickened Sludge (mg/kg)	Sludge TCLP. Extract (µg/ℓ)
Classical Pollutants								
ammonia, as N	NA	46	100	19	62	55	6,300	NA
BOD-5 Day (carbonaceous)	NA	3,200	380	2,200	260	440	NA	NA
chemical oxygen demand	NA	7,100	1,500	7,300	1,400	1,400	NA	NA
cyanide, total*	NA	0.032	--	--	--	--	14	NA
fluoride	NA	0.71	0.60	0.68	0.63	0.63	NA	NA
nitrate-nitrite, as N	NA	1.3	0.59	5.1	0.56	0.58	33	NA
nitrogen, kjeldahl, total	NA	300	160	230	130	120	100,000	NA
oil and grease, total recoverable	NA	39c	17c	54c	11c	16c	NA	NA
residue, filterable	NA	4,900	2,400	4,100	3,300	3,400	NA	NA
residue, non-filterable	NA	1,100	310	780	190	180	NA	NA
sulfide, total (iodometric)	NA	11c	7.1c	16c	7.6c	3.5c	NA	NA
total organic carbon	NA	1,900	410	1,400	530	500	NA	NA
total phosphorus, as P	NA	8.0	4.5	6.4	2.9	2.5	NA	NA
corrosivity (MPY)	NA	NA	NA	NA	NA	NA	<10	NA
flash point (°C)	NA	NA	NA	NA	NA	NA	60	NA
pH, soil	NA	NA	NA	NA	NA	NA	6.8	NA
residue, total (%)	NA	NA	NA	NA	NA	NA	6.9	NA
residue, total volatile (%)	NA	NA	NA	NA	NA	NA	86	NA
sulfide, total (Monier-Williams)	NA	NA	NA	NA	NA	NA	620	NA

TABLE III-21 (continued)

Pollutant Category and Pollutant	Tap Water	Wastewater-Day 1		Wastewater-Day 2			Sludge	
		Raw Waste	Treated Effluent	Raw Waste	Treated Effluent	Treated Effluent**	Thickened Sludge	TCLP Extract
Field Measurements								
flow (mgd)	NA	0.7a	0.7a	0.7a	0.7a	0.7a	NA	NA
conductivity (umhos)	NA	4410-6470	4290-4940	4900-5790	5020-5110	5020-5110	NA	NA
pH	NA	5.9-9.0	7.7-8.1	7.1-10.7	7.8	7.8	NA	NA
settleable solids (mg/ℓ)	NA	140	16	46	Trace	Trace	NA	NA
temperature (°C)	NA	15.4-31.0	35.0-39.0	29.3-33.0	32.6-39.0	32.6-39.0	NA	NA

* Priority pollutants.
-- Indicates pollutant concentration below detection limit.
NA Indicates not analyzed.
a Average daily flow.
c Average of grab sample results.
t Denotes tentative identification below the detection limit.
DET Indicates pollutant concentration qualitatively detected.
** A duplicate of the Day 2 effluent wastewater sample was taken as part of the ongoing QA/QC program.

f. Plant 88888. This plant produces products by fermentation and chemical synthesis (Subcategories A and C). Approximately 1.0 mgd of wastewater is treated in the treatment system before discharge to the river.

Between January and July 1987, EPA conducted a pilot study at Plant 88888 to evaluate COD removal, as well as aquatic toxicity and specific organic compound removal from pharmaceutical wastewater by the use of PAC addition to biological treatment systems. Samples of the raw wastewater, pilot plant effluent, and pilot plant mixed liquors, were analyzed for selected volatile and semivolatile organic compounds. Acetone and acrylonitrile were the specific VOCs, and alpha-picoline and 4-nitroaniline were the specific SVOCs, analyzed for in the January and March samples. Results of these analyses are listed in Table III-22. The high concentration of acetone in the January sample required that the sample be diluted prior to analysis. This resulted in a high quantification limit for acrylonitrile.

Based on results of a computer search of data types from the January and March samples, alpha-picoline and dicyclohexylamine were selected as the specific SVOCs, and acetone, acrylonitrile, ethyl acetate, ethyl benzene, and total xylenes were selected as the specific VOCs to be analyzed for in May and June. Methylene chloride was also added to the VOC list because it was thought to be used at the plant.

Analytical results of the samples collected in May and June are also listed in Table III-22. High concentrations of total xylenes were found in all of the raw wastewater samples. These high concentrations required that the samples be greatly diluted before analysis resulting in high detection limits for the other compounds.

g. Summary of Analytical Results. Analytical results from recent sampling done at Plants 12135, 12204, 12236, 12447, 88888, and 99999 are summarized in Table III-23.

Priority Pollutant VOCs. The list of 17 VOCs detected in the pharmaceutical industry's wastewater during the ITD/RCRA sampling program is virtually identical to the list of those found in the screening and verification sampling program (see Table III-23). Only three compounds were detected in the ITD/RCRA program that were not found in the screening and verification sampling program: acrylonitrile; 1,1-dichloroethane; and trans-1,2-dichloroethene. However, these three compounds were neither detected frequently nor at high concentrations. The remaining 14 compounds detected in the industry wastewater during the ITD/RCRA sampling were found less frequently or at lower levels than in the screening and verification program.

TABLE III-22
SUMMARY OF ANALYTICAL RESULTS FOR SPECIFIC
ORGANIC COMPOUNDS AT PLANT 88888

Pollutant Category and Pollutant	Raw Wastewater (µg/ℓ)									
	1/14/87	3/18/87	5/4/87	5/5/87	5/11/87	5/13/87	6/14/87	6/16/87	6/18/87	6/22/87
Volatile Organics										
acrylonitrile*	<10,000	<50	<63,000	<25,000	<63,000	<63,000	<63,000	<13,000	<13,000	<25,000
ethylbenzene*	NA	NA	28,000	13,000	<32,000	<13,000	25,000	39,000	17,000	46,000
methylene chloride*	NA	NA	<63,000	<25,000	<63,000	<63,000	<63,000	<13,000	<13,000	<25,000
acetone	33,000	330	<63,000	<25,000	<63,000	<63,000	<63,000	34,000	87,000	180,000
ethyl acetate	NA	NA	<130,000	<50,000	<130,000	<130,000	<130,000	<25,000	<25,000	<50,000
total xylenes	NA	NA	150,000	68,000	160,000	46,000	150,000	220,000	88,000	300,000
Semivolatile Organics										
alpha-picoline	300,000	58,000	6,400	7,300	7,100	330,000	200,000	39,000	5,300	2,200
dicyclohexylamine	NA	NA	1,000	420	360	24,000	13,000	39,000	28,000	6,800
4-nitroaniline	<2,000	<500	NA	NA	NA	NA	NA	NA	NA	NA

* Priority pollutants.
NA Indicates not analyzed.

TABLE III-23
SUMMARY OF DETECTED ANALYTICAL RESULTS
ITD LISTED COMPOUNDS

Pollutant Category/ Pollutant	Raw Wastewater: Total Number of Samples	Raw Wastewater: Total Number of Detected Analyses	Raw Wastewater: Concentration Range (µg/ℓ)	Raw Wastewater: Average Concentration (µg/ℓ)	Raw Wastewater: Median (µg/ℓ)	Treated Effluent: Total Number of Samples	Treated Effluent: Total Number of Detected Analyses	Treated Effluent: Concentration Range (µg/ℓ)	Treated Effluent: Average Concentration (µg/ℓ)	Treated Effluent: Median (µg/ℓ)	Comments
Volatile Organics											
acrolein*	7	1	75	75	75	5	0	--	--	--	Indirect discharger
acrylonitrile*	7	1	136	136	136	5	0	--	--	--	Indirect discharger
benzene*	7	2	17-24	21	21	5	1	31	31	31	Indirect discharger
carbon tetrachloride*	2	0	--	--	--	2	1	42	--	--	Direct discharger
chlorobenzene*	7	1	19	19	19	5	0	--	--	--	Indirect discharger
chloroform*	7	5	50-8,030	2,759	596	5	3	51-97	70	62	Indirect discharger
1,1-dichloroethane*	7	1	76	76	76	5	1	30	30	30	Indirect discharger
1,1-dichloroethene*	7	1	22	22	22	5	0	--	--	--	Indirect discharger
1,2-dichloroethane*	7	3	31-2,497	922	239	5	0	--	--	--	Indirect discharger
trans-1,2-dichloroethene*	7	1	442	442	442	5	1	25	25	25	Indirect discharger
ethylbenzene*	7	2	136-659	398	398	5	0	--	--	--	Indirect discharger
	10	7	13,000-46,000	28,600	28,000	2	0	--	--	--	Direct Discharger
methylene chloride*	7	5	2,086-14,959	5,868	4,696	5	3	113-5,167	1,819	176	Indirect discharger
	10	2	114-10,745	5,430	5,430	2	2	21-158	90	90	Direct discharger
tetrachloroethene*	7	1	43	43	43	5	0	--	--	--	Indirect discharger
toluene*	7	6	33-8,482	2,527	1,035	5	2	362-7,896	4,129	4,129	Indirect discharger
	2	0	--	--	--	2	1	19	19	19	Direct discharger
1,1,1-trichloroethane*	7	2	87-393	240	240	5	1	62	62	62	Indirect discharger
trichloroethene*	7	1	87	87	87	5	0	--	--	--	Indirect discharger
vinyl chloride*	7	1	42	42	42	5	0	--	--	--	Indirect discharger
acetone	7	5	4,592-797,020	222,820	133,239	5	4	104-110,395	28,215	1,180	Indirect discharger
	12	6	330-180,000	56,000	33,500	2	2	96-174	135	135	Direct discharger
2-butanone (MEK)	7	4	742-2,031	1,352	1,318	5	0	--	--	--	Indirect discharger
diethyl ether	7	2	287-16,627	8,457	8,457	5	2	530-14,288	7,409	7,409	Indirect discharger
2-hexanone	2	0	--	--	--	2	1	1,087	1,087	1,087	Direct discharger
isobutyl alcohol	7	2	881-1,557	1,219	1,219	5	0	--	--	--	Indirect discharger
vinyl acetate	6	1	99	99	99	5	1	63	63	63	Indirect discharger
Semivolatile Organics											
benzidine*	7	1	205	205	205	5	2	192-224	208	208	Indirect discharger
bis(2-chloroethyl)ether*	7	1	11	11	11	5	0	--	--	--	Indirect discharger
bis(2-ethylhexyl) phthalate*	7	0	--	--	--	5	1	22	22	22	Indirect discharger
4-chloro-3-methylphenol*	7	1	148	148	148	5	0	--	--	--	Indirect discharger
2-chloro-naphthalene*	7	4	37-183	74	38	5	3	38-44	40	39	Indirect discharger
1,2-dichlorobenzene*	7	1	2280	2280	2280	5	0	--	--	--	Indirect discharger
3,3-dichlorobenzene*	7	1	87	87	87	5	0	--	--	--	Indirect discharger
2,6-dinitrotoluene*	7	1	191	191	191	5	0	--	--	--	Indirect discharger
isophorone*	7	1	84	84	84	5	0	--	--	--	Indirect discharger
n-nitrosodi-n-propylamine*	7	1	45	45	45	5	1	82	82	82	Indirect discharger

TABLE III-23 (continued)
ITD/RCRA SAMPLING PROGRAM
SUMMARY OF DETECTED ANALYTICAL RESULTS

Pollutant Category/ Pollutant	Raw Wastewater					Treated Effluent					Comments
	Total Number of Samples	Total Number of Detected Analyses	Concentration Range (µg/ℓ)	Average Concentration (µg/ℓ)	Median (µg/ℓ)	Total Number of Samples	Total Number of Detected Analyses	Concentration Range (µg/ℓ)	Average Concentration (µg/ℓ)	Median (µg/ℓ)	
2-nitrophenol*	7	1	28	28	28	5	0	--	--	--	Indirect discharger
phenol*	7	0	--	--	--	5	1	124	124	124	Indirect discharger
alpha-picoline	12	10	2,200-330,000	95,500	23,000	2	0	--	--	--	Direct discharger
alpha-terpineol	7	2	14-15	15	15	5	0	--	--	--	Indirect discharger
benzoic acid	7	1	187	187	187	5	0	--	--	--	Indirect discharger
o-cresol	7	1	23	23	23	5	0	--	--	--	Indirect discharger
p-cresol	7	1	18	18	18	5	0	--	--	--	Indirect discharger
diphenyl ether	7	1	14	14	14	5	0	--	--	--	Indirect discharger
n-docosane	7	1	61	61	61	5	0	--	--	--	Indirect discharger
n-dodecane	7	0	--	--	--	5	2	24-28	26	26	Indirect discharger
n-eicosane	7	2	206-212	209	209	5	3	142-296	208	187	Indirect discharger
n-hexacosane	7	1	189	189	189	5	0	--	--	--	Indirect discharger
n-hexadecane	7	1	22	22	22	5	0	--	--	--	Indirect discharger
hexanoic acid	7	2	11-146	79	79	5	0	--	--	--	Indirect discharger
2-methylnaphthalene	6	0	--	--	--	5	2	484-754	619	619	Indirect discharger
b-naphthylamine	7	1	68	68	68	5	0	--	--	--	Indirect discharger
n-octacosane	7	1	29	29	29	5	0	--	--	--	Indirect discharger
n-triacontane	7	0	--	--	--	5	1	81	81	81	Indirect discharger
Pesticides/Herbicides											
BHC, alpha*	5	0	--	--	--	3	1	6.2	6.2	6.2	Indirect discharger
BHC, beta*	5	1	1.198	1.198	1.198	3	2	2.2	2.0	0.45	Indirect discharger
BHC, delta*	5	1	0.012	0.012	0.012	3	0	--	--	--	Indirect discharger
4,4'DDD	5	1	0.914	0.914	0.914	3	0	--	--	--	Indirect discharger
endrin ketone	5	1	1.2	1.2	1.2	3	0	--	--	--	Indirect discharger
TEPP	4	1	4,110	4,110	4,110	3	2	780-1,154	967	967	Indirect discharger
Metals											
antimony*	7	2	11-15	13	13	5	0	--	--	--	Indirect discharger
arsenic*	7	4	6.4-18	12	12	5	3	7.9-14	11	12	Indirect discharger
cadmium*	7	2	5-8	7	7	5	0	--	--	--	Indirect discharger
chromium*	7	7	12-99	39	18	5	3	4-30	21	30	Indirect discharger
	2	2	18-26	22	22	2	1	22	22	22	Direct discharger
copper*	7	7	45-500	201	160	5	5	29-71	44	36	Indirect discharger
lead*	7	1	13	13	13	5	0	--	--	--	Indirect discharger
mercury*	7	1	0.4	0.4	0.4	5	0	--	--	--	Indirect discharger

TABLE III-23 (continued)
ITD/RCRA SAMPLING PROGRAM
SUMMARY OF DETECTED ANALYTICAL RESULTS

Pollutant Category/ Pollutant	Raw Wastewater					Treated Effluent					Comments
	Total Number of Samples	Total Number of Detected Analyses	Concentration Range (µg/ℓ)	Average Concentration (µg/ℓ)	Median (µg/ℓ)	Total Number of Samples	Total Number of Detected Analyses	Concentration Range (µg/ℓ)	Average Concentration (µg/ℓ)	Median (µg/ℓ)	
nickel*	7	4	33-66	51	52	5	3	19-27	23	23	Indirect discharger
	2	1	41	41	41	2	0	--	--	--	Direct discharger
selenium*	7	3	12-16	13	12	5	2	8.3-10	9	9	Indirect discharger
silver*	7	1	2.1	2.1	2.1	5	0	--	--	--	Indirect discharger
zinc*	7	7	100-330	249	303	5	5	26-181	86	60	Indirect discharger
	2	2	117-164	141	141	2	2	20-50	35	35	Direct discharger
aluminum	6	6	270-3,200	1,915	2,225	5	5	630-1,740	962	799	Indirect discharger
	2	2	118-178	60	60	2	0	--	--	--	Direct discharger
barium	7	6	57-140	107	117	5	5	33-88	58	33	Indirect discharger
	2	1	218	218	218	2	0	--	--	--	Direct discharger
boron	6	4	77-210	131	119	5	3	75-100	86	84	Indirect discharger
	2	1	209	209	209	2	0	--	--	--	Direct discharger
calcium	6	6	100,000-309,000	181,500	165,000	5	5	98,000-274,000	160,200	100,000	Indirect discharger
	2	2	51,500-51,700	51,600	51,600	2	2	51,200-63,700	57,450	57.450	Direct discharger
cobalt	7	3	4-55	28	26	5	0	--	--	--	Indirect discharger
iron	7	7	2,000-8,100	3,386	2,700	5	5	630-1,020	756	720	Indirect discharger
	2	2	121,000-171,000	146,000	146,000	2	2	4130-5710	4920	4920	Direct discharger
lithium	7	2	1,140	1,140	1,140	5	0	NA	NA	NA	Indirect discharger
magnesium	6	6	14,000-39,400	26,533	25,000	5	5	17,000-23,400	19,480	18,000	Indirect discharger
	2	2	1680-1810	1,745	1,745	2	2	1,340-1,440	1,390	1,390	Direct discharger
manganese	6	6	83-3,200	907	475	5	5	39-205	104	50	Indirect discharger
	2	2	794-1,380	1,087	1,087	2	2	222-255	239	239	Direct discharger
osmium	7	0	--	--	--	5	0	--	--	--	Indirect discharger
	2	1	100e	100	100	2	2	200e-300e	250	250	Direct discharger
sodium	6	6	273,000-2,800,000	1,010,500	845,000	5	5	238,000-780,000	540,400	660,000	Indirect discharger
	2	2	1,530,000-1,720,000	1,625,000	1,625,000	2	2	1,410,000-1,650,000	1,530,000	1,530,000	Direct discharger
strontium	7	3	410	410	410	5	0	NA	NA	NA	Indirect discharger
titanium	6	4	15-59	42	47	5	3	100	100	100	Indirect discharger
	2	2	85-126	106	106	2	0	ND	ND	ND	Direct discharger
vanadium	7	2	7-9	8	8	5	1	ND-4	1	0	Indirect discharger
	2	2	86-129	108	108	2	0	ND	ND	ND	Direct discharger
Classicals											
cyanide, total*	7	1	32	32	32	5	0	--	--	--	Indirect discharger
	NR	NR	--	--	--	2	2	25-29	27	27	Direct discharger
BOD (mg/ℓ)	7	7	1,300-4,600	2,757	2,200	5	5	260-440	362	380	Indirect discharger
	2	2	1,300-2,300	1,800	1,800	2	2	20-24	22	22	Direct discharger

TABLE III-23 (continued)
ITD/RCRA SAMPLING PROGRAM
SUMMARY OF DETECTED ANALYTICAL RESULTS

Pollutant Category/ Pollutant	Raw Wastewater					Treated Effluent					Comments
	Total Number of Samples	Total Number of Detected Analyses	Concentration Range (µg/ℓ)	Average Concentration (µg/ℓ)	Median (µg/ℓ)	Total Number of Samples	Total Number of Detected Analyses	Concentration Range (µg/ℓ)	Average Concentration (µg/ℓ)	Median (µg/ℓ)	
COD (mg/ℓ)	7	7	3,600-10,000	6,593	7,100	5	5	800-1,500	1,180	1,400	Indirect discharger
	2	2	2,200-2,300	2,250	2,250	2	2	380-400	390	390	Direct discharger
TSS (mg/ℓ)	7	7	64-2,300	1,321	1,400	5	5	180-310	240	220	Indirect discharger
	2	2	340-530	435	435	2	2	59-66	63	63	Direct discharger

* Priority pollutant.
-- Not detected.
NR No value reported due to matrix interference.
e Estimated value.

The priority pollutant VOCs that continue to be detected frequently in the industry raw wastewater at miiigram-per-liter levels are those previously identified as commonly used solvents and/or extractive agents in pharmaceutical manufacturing operations (e.g., chloroform, 1,2-dichloroethane, methylene chloride, and toluene).

Nonconventional Pollutant VOCs. Acetone was detected in the raw wastewater of five of the six facilities sampled (i.e., Plants 12135, 12204, 12236, 88888, and 99999). Information obtained from the sixth facility (i.e., Plant 12447) indicates that acetone is used as a solvent in the manufacture of pharmaceuticals; however, it is not known if acetone was being used during the sampling episode. Patent search information indicates that all plants except Plant 12336 are likely to be using acetone as a process solvent in pharmaceutical product manufacture. According to solvent-use information presented in Table III-6, acetone is commonly used, and is ranked fourth in terms of tons of organic solvents used annually by the industry.

Methyl ethyl ketone (MEK, or 2-butanone) was found in the raw wastewater of three plants (i.e., Plants 12135, 12447, and 99999). Available solvent-use information confirms that MEK is used as process solvent at Plant 12447, and indicates that it is not used at Plant 99999. It is not known if MEK is used as a process solvent at Plant 12135. According to industry solvent-use information, MEK is commonly used, and is ranked sixteenth in terms of tons of organic solvents used annually by the industry.
Diethyl ether (ethyl ether) was found in the raw wastewater of Plants 12135 and 12204. Solvent-use information is not available for Plant 12135, but for Plant 12204, it does not indicate the use of diethyl ether in chemical synthesis or fermentation operations. Information presented in Table III-6 indicates that, in terms of annual usage, ethyl ether is the most commonly used organic solvent in the pharmaceutical industry.

Methyl butyl ketone (2-hexanone) was found in one final effluent sample from Plant 12236. Plant officials indicate that it is not used as a raw material and they are not sure of the source. Methyl butyl ketone is not known to be commonly used in the manufacture of pharmaceutical products.

Isobutyl alcohol was found in both raw wastewater samples collected at Plant 12447. Plant officials indicate that isobutyl alcohol is not used in chemical synthesis or fermentation operations. Isobutyl alcohol is not known to be an organic solvent commonly used by this industry. However, isobutyl alcohol is known to be produced by the fermentation of carbohydrates.

Vinyl acetate was found in raw wastewater and pretreated effluent sampled at Plant 12204 at levels less than 100 ppb. Organic solvent-use information for Plant 12204 does not indicate the use

of vinyl acetate in chemical synthesis or fermentation operations. Vinyl acetate is not known to be commonly used as an organic solvent in this industry. The process source of this compound should be investigated further.

Priority Pollutant SVOCs. ITD/RCRA sampling results added seven compounds to the group of priority pollutants detected in the industry wastewater in EPA sampling efforts: benzidine, bis(2-chloroethyl)ether, 4-chloro-3-methylphenol, 2-chloronaphthalene, 3,3'-dichlorobenzene, 2,6-dinitrotoluene, and n-nitrosodi-n-propylamine. Only 2-chloronaphthalene was detected with any significant frequency, and only 1,2-dichlorobenzene was detected at a concentration above 500 ppb. in raw wastewater. Dichlorobenzene was found in the raw wastewater of Plant 12135 only. Dichlorobenzene is a common solvent, and 308 Portfolio information indicates that Plant 12135 uses 1,2-dichlorobenzene as a raw material. Efforts to identify the process source of the rest of the remaining SVOCs should be conducted.

Nonconventional Pollutant SVOCs. Fifteen SVOCs were detected in the industry wastewater; however, only alpha-picoline and n-eicosane were found with significant frequency or at high levels. The process source of these compounds should be investigated further.

Priority Pollutant Pesticides and Herbicides. In the recent sampling effort, low levels of alpha and beta BHC were found in the biologically pretreated effluent from Plant 99999, a plant known to produce some pesticides. Low levels of beta and delta BHC were found in the raw wastewater of Plant 12135; however, the source is not known. The 308 Portfolio information does not indicate that either plant uses alpha, beta, or delta BHC as a raw material. The presence of pesticides in wastewater appears to be from non-pharmaceutical manufacturing operations; however, the source of these pesticides should be definitely established.

Nonconventional Pollutant Herbicides and Pesticides. Eight herbicides and pesticides were detected in the industry wastewater in the recent sampling effort. Only tetraethylpyrophosphate (TEPP) was found with any significant frequency and at high levels: at Plant 99999. Plant 99999 is known to produce some pesticides as well as pharmaceutical products. It is not known if the plant was manufacturing pesticides during the sampling episode. Efforts should be conducted to establish the source of the pesticides and herbicides detected.

Priority Pollutant Metals. The metals detected in the ITD/RCRA sampling program were found at levels within, or lower than, the range found in the screening and verification sampling program. Effluent concentrations of priority pollutant metals found during the screening and verification sampling program were below treatable levels; as a result, development of national limitations and standards was not warranted.

Nonconventional Pollutant Metals. Only the more common ions (i.e., calcium, iron, magnesium, and sodium) were detected with significant frequency and at high levels (see Table III-23). High levels of calcium and/or sodium were expected in raw wastewater samples, as either lime ($Ca(OH)_2$) or sodium hydroxide (NaOH) is commonly used as a neutralizing agent.

Cyanide. Cyanide is known to be used as a raw material in the manufacture of certain pharmaceuticals. During the ITD/RCRA sampling program, cyanide was found in the wastewater from the two plants (i.e., Plants 12236 and 99999) known to be using it, or have used it in the past, as a raw material in the manufacture of pharmaceuticals. As part of the National Pollutant Discharge Elimination System (NPDES) permit requirement, Plant 12236 routinely monitors cyanide levels in treated effluent.

D. POLLUTANT MASS LOADINGS AND SOLID WASTE GENERATION

1. Wastewater

An attempt was made to estimate the total mass discharge of conventional, priority, and nonconventional pollutants in the wastewater of the pharmaceutical manufacturing industry. To provide a basis for comparison, estimates were developed from previously available data (i.e., 308 Questionnaire, screening and verification program, and OAQPS data bases) and from the recently acquired sampling data (i.e., from Plants 12135, 12204, 12236, 12447, and 99999).

Mass load estimates were developed for the raw wastewater and final effluents for both direct and indirect dischargers in the pharmaceutical manufacturing industry. Also, the mass loadings were divided between two types of plants: those conducting Subcategory A, B, and C operations (ABC), and those conducting only Subcategory D operations. To avoid confusion and to provide a basis for comparison of estimates developed from various data bases, only the total raw waste load estimates by major pollutant category are presented in this section. Detailed mass load estimates categorized by discharge and plant type are appended.

a. 308 Questionnaire Data Base. Analytical results reported by each pharmaceutical plant in the 308 Questionnaire responses are the best available data for estimating total mass discharge of conventional pollutants (BOD and TSS), and the nonconventional pollutant (COD).

For direct dischargers, raw waste and final effluent mass loadings were calculated on a plant-by-plant basis. The long-term average flow and pollutant average concentrations provided in the 308 Questionnaire responses, assuming 365 operating days per year, were used. Subcategory average flow, BOD_5, TSS, and COD values were used when plant-specific data were not available.

For indirect dischargers, mass loading estimates were developed using subcategory average BOD5, COD, TSS values for each plant because very few of the 285 indirect dischargers provided BOD, COD, and TSS values in the 308 Questionnaire responses. Very few plants have pretreatment systems in place that would reduce the raw waste discharge levels. Therefore, no attempt was made to estimate any difference between the total industry raw waste mass loading and the estimated discharges to POTWs.

The estimated annual raw waste loadings for BOD5, COD, and TSS, developed from the 308 Questionnaire data base, are summarized in Table III-24. The detailed mass load estimates categorized by discharge and plant type are presented in Appendix I.

b. Screening and Verification Data Base. Analytical results from the 26 pharmaceutical plants involved in the Screening and Verification Sampling Program are the best available data for developing rough estimates of the annual mass discharge of priority pollutants in pharmaceutical manufacturing industry wastewater. Annual mass loadings were computed for each priority pollutant detected in the Screening and Verification Sampling Program by calculating the product of the pollutant mean concentration, reported in Table III-11, and the total industry flow expected to contain the pollutant: mean (mg/l) x flow (mgd) x 8.345 (conversion factor) x 365 (days/year). A plant's flow was used in the total flow estimate if: (1) 308 Portfolio or product patent information indicated that the plant used or was likely to use the pollutant in question in the manufacture of pharmaceuticals, or (2) the pollutant in question was detected in wastewater according to the 308 Portfolio, the Screening and Verification Sampling Program, or the TTVO Questionnaire.

Estimated annual raw waste priority pollutant loadings by major pollutant category are summarized in Table III-24. Detailed backup for the raw waste estimates, as well as for final effluent estimates, is presented in Appendix J.

c. OAQPS Data Base. Total industry mass discharge estimates for priority and nonconventional VOCs were also estimated from the data obtained by OAQPS in the 1975 and 1985 VOC disposition surveys (see Tables III-6 and III-8).

Table III-6 presents a compilation of the 1975 survey results. Twenty-six PMA member companies reported these data, which they felt represented 85 percent of the VOCs used in their operations. These reporting companies accounted for approximately 53 percent of the 1975 domestic sales of ethical pharmaceuticals. Total industry mass discharge estimates were developed by assuming the mass of pollutants sewered according to the survey represented only 53 percent of the total.

TABLE III-24

ESTIMATED ANNUAL RAW WASTE LOADINGS
PHARMACEUTICAL MANUFACTURING INDUSTRY

Pollutant Group	Estimated Annual Raw Waste Loading (1000 lbs/yr)					
	308 Questionnaire Data Base[1]	Screening/ Verification Data Base[2]	QAQPS Data Base[3]	ITD/RCRA Data Base[4]		
				Method A	Method B	Method C
Conventional Pollutants						
o BOD5	261,700	--	--	510,000	510,000	510,000
o TSS	113,700	--	--	250,000	250,000	250,000
Priority Pollutants						
o Volatile Organics	--	4,658	7,800	1,200	1,300	2,200
o Semivolatile Organics	--	543	--	37	1,100	630
o Pesticides	--	0.02	--	0.035	0.62	0.42
o Metals	--	114.2	--	82	120	105
o Cyanide	--	26.9	--	0.33	4.1	6.3
Nonconventional Pollutants						
o COD	634,500	--	--	1,100,000	1,100,000	1,100,000
o Volatile Organics						
ITD Listed	--	--	11,000	16,000	16,000	29,000
Non-ITD Listed	--	--	40,800	--	--	--
o Semivolatile Organics	--	--	--	26	863	181
o Pesticides/Herbicides	--	--	--	112	192	411

* Excluding xylenes
[1] Back-up calculations supporting these estimates can be found in Appendix I.
[2] Back-up calculations supporting these estimates can be found in Appendix J.
[3] Back-up calculations supporting these estimates can be found in Appendix K.
[4] Back-up calculations supporting these estimates can be found in Appendix L.

Table III-8 presents results from the 1985 VOC disposition survey. The data were obtained from 22 PMA member companies that accounted for approximately 70 percent of pharmaceutical sales in 1985. Total industry mass discharge estimates were developed by assuming the mass of pollutants sewered according to the survey represented only 70 percent of the total.

Estimated annual raw waste loadings for the priority and nonconventional pollutant VOCs are also summarized in Table III-24. Detailed backup for the raw waste estimates is presented in Appendix K. Information was not available to categorize the estimates by discharge or plant type.

d. ITD/RCRA Data Base. Analytical results from recent sampling done at Plants 12135, 12204, 12236, 12447, and 99999 were used to develop rough estimates of the annual mass discharges of ITD-listed pollutants from pharmaceutical manufacturing facilities. The mass loadings were estimated by three methods. In each approach, industry average concentrations were developed for all pollutants found at concentrations above their analytical detection limit. The average concentrations were then used to calculate the total industry loadings, using an estimate of the total industry flow: average pollutant concentration (mg/l) x flow (mgd) x 8.345 (conversion factor) x 365 (days/year).

The differences between the three approaches are in the methods used to calculate the individual pollutant average concentrations:

- For Method A, individual pollutant average concentrations were developed assuming "not detected" observations equal to zero.

- For Method B, individual pollutant average concentrations were developed assuming "not detected" observations equal to the analytical detection limit.

- For Method C, individual pollutant average concentrations were developed including only observations reported above the analytical detection limit.

Method A is a "best case" calculation for the average concentration since the not detected observations are perceived as being at the lowest possible concentration. Method B is a "worst case" calculation for the average concentration since the not detected observations are perceived as being the highest possible concentration. Method C uses a "censored" data base for the calculation of the average concentration. Method C is worst than a "worst case" calculation for the average concentration since it assumes that the pollutants are found at levels above their analytical detention limits in all samples at all facilities. Actual industry mass loadings would be expected to be between the levels predicted by Methods A and B.

Raw waste mass loading estimates were developed by plant type (i.e., ABC, and D) for both indirect and direct discharging facilities by estimating the wastewater flows for each group separately. No estimations were made for treated effluents from direct and indirect discharging facilities because of the extremely limited pollutant treatability and/or removal data provided by the ITD/RCRA sampling program. The total annual flow estimate for direct-discharging Subcategory ABC pharmaceutical plants is based on the total flow from 30 facilities (21,381,000 gpd). The total annual flow estimate for direct-discharging Subcategory D plants is based on the total flow from 21 facilities (3,540,000 gpd). The Subcategory ABC indirect discharger total annual flow estimate is based on total flow from 130 plants (31,144,000 gpd). The total annual flow estimate for
indirect-discharging Subcategory D plants is based on total flow from 155 facilities (8,826,000 gpd). All plants were assumed to be operating 365 days per year.

EPA recognizes that these mass loading estimates are rough because the industry average pollutant concentrations were developed from a limited data base, and the plants sampled were not selected at random.

The annual raw waste mass discharge of conventional, priority, and nonconventional pollutants for the pharmaceutical manufacturing industry for Methods A, B, and C is shown in Table III-24. Calculations supporting these estimates are presented in Appendix L.

e. Discussion.

Conventional Pollutants. The best estimates of conventional pollutant discharges (i.e., BOD_5 and TSS) are those developed from the 308 Questionnaire data base. These estimates were developed with actual long-term average data for each pharmaceutical plant (where available); subcategory average values were used for plants when data were not available.

Priority Pollutants. The best estimates of priority-pollutant mass discharge by the pharmaceutical manufacturing industry are those derived from results obtained during the Screening and Verification Sampling Program. These estimates incorporate plant-by-plant priority-pollutant use information obtained from the 308 Questionnaire with mean priority-pollutant wastewater concentrations from sampling 26 pharmaceutical plants.

Nonconventional Pollutants. The best estimate of the discharge of the nonconventional pollutant COD is that developed from the 308 Questionnaire data base. This estimate was developed with actual long-term average data for each plant (when available); subcategory average values for plants were used when data were not available. The best estimates of the discharge of nonconventional pollutant VOCs, SVOCs, and pesticides are those developed by Method B from the ITD/RCRA data base. However, the VOCs and pesticides estimates generated by Methods A and B are not significantly different as the

analytical detection limit for these compounds are not significantly greater than zero.

2. Solid Waste Generation and Disposal

Wastewater treatment facilities at pharmaceutical manufacturing plants produce both primary and biological sludges that are usually dewatered prior to disposal. The amount of wastewater treatment sludge generated at each facility depends on a number of conditions, including (1) raw waste characteristics; (2) the existence, efficiency, and/or type of primary treatment; (3) type of biological treatment system employed; and (4) efficiency of biological solids removal from the wastewater.

Total industry sludge generation was estimated based on information from each plant's 308 Portfolio (when available). When data were not available, rough estimates were made of solids generated from an activated sludge treatment system.

It is estimated that the wastewater treatment systems at direct discharging facilities generate 42 million pounds (dry basis) of wastewater treatment plant sludge annually. This estimate does not include an estimate for Plant 12256. Sufficient information was not available to determine how much of the sludge generated at Plant 12256, as indicated in their 308 Questionnaire, was related to pharmaceutical manufacturing operations. It is estimated that an additional 7 million pounds (dry basis) of wastewater treatment plant sludge is generated at indirect discharging facilities.

a. Sludge Characteristics. The data collected by EPA in the recent sampling program are the only data available for characterizing wastewater treatment plant sludge generated by the industry. Wastewater treatment plant sludge samples were collected both before and after dewatering operations. Analytical results are summarized in Table III-25. Sludge analyses were conducted for most of the ITD-listed compounds.

Only the sludge from Plant 12236 is known to be disposed of in a hazardous waste landfill. Plant 12204 composts primary and secondary sludges and sells it as soil conditioner. Plant 99999 uses a contract hauler to dispose of waste sludge.

Sludge samples were also analyzed using the Toxicity Characteristic Leaching Procedure (TCLP). The sludge leachate produced by the TCLP was also analyzed for most of the pollutants on the ITD list. Results are shown in Table III-25, as well as the proposed toxicity characteristic regulatory levels.

None of the sludges exhibited the characteristic of toxicity based on the proposed and final levels. However, primary sludge at Plant 12204 has the potential for exhibiting the characteristic of corrosivity with a pH greater than 12.5.

TABLE III-25
SUMMARY OF ANALYTICAL RESULTS FOR SLUDGE SAMPLES
ITD/RCRA SAMPLING PROGRAM

	Plant 12204					Plant 12236			Plant 99999		
	Primary Sludge			Secondary Sludge		Combined Sludge			Secondary Sludge		Regulatory
	Thickened (mg/kg)	Dewatered (mg/kg)	TCLP (µg/ℓ)	Dewatered (mg/kg)	TCLP (µg/ℓ)	Thickened (mg/kg)	Dewatered (mg/kg)	TCLP (µg/ℓ)	Dewatered (mg/kg)	TCLP (µg/ℓ)	Levels (µg/ℓ)
Volatile Organics											
acrolein*	--	--	--	--	102	--	--	--	--	--	--
1,1-dichloroethane*	--	--	--	0.155	21	--	0.045	20	--	--	--
trans-1,2-dichloroethene*	0.236	--	--	0.114	25	--	--	--	--	--	--
methylene chloride*	7.109	0.929	63	--	52	--	--	--	--	--	8,600(p)
toluene*	0.500	--	--	0.100	37	--	0.077	140	1.406	79	14,400(p)
acetone	504.209	282.229	14,081	66.955	17,028	--	0.555	--	--	--	--
diethyl ether	--	2.368	61	--	--	--	--	--	--	--	--
ethylbenzene	--	--	--	--	--	--	--	--	1.145	--	--
isobutyl alcohol	--	--	--	--	140	--	--	--	--	--	--
methacrylonitrile	--	--	--	--	--	--	0.191	106	--	--	--
methyl ethyl ketone	--	--	--	--	980	--	--	--	--	--	7,200(p)
Semivolatile Organics											
bis(2-chloroethyl)ether*	--	--	--	--	--	--	3.350	--	--	--	50(p)
2-chloronaphthalene*	--	--	--	--	--	--	--	--	58.855	44	--
phenol*	19.800	2.079	15	--	--	--	--	--	--	--	14,400(p)
benzoic acid	--	--	--	--	--	--	--	--	--	65	--
2-methylnaphthalene	--	--	--	--	--	--	--	--	582.725	--	--
2(methyl thio)benzathiazole	--	--	--	--	--	--	--	--	--	11	--
n-eicosane	--	--	--	--	--	--	--	--	340.855	72	--
n-octadecane	--	--	--	--	--	--	2.036	--	--	--	--
Metals											
antimony*	--	--	--	--	--	53	6	--	--	--	--
beryllium*	--	1	--	0.5	--	--	--	--	--	--	--
cadmium*	--	--	--	2	--	--	17	15	--	--	1,000(f)
chromium*	2	5	--	6	--	10	10	--	--	--	5,000(f)
copper*	20	41	219	44	--	--	26	--	185	--	--
lead*	--	--	--	16	--	--	--	--	--	--	5,000(f)
mercury*	0.9	0.3	0.4	0.9	--	2.5	1.6	--	--	--	200(f)
nickel*	2	5	--	10	--	--	19	85	--	--	--
silver*	0.6	1.8	--	1.8	--	--	2	--	--	--	5,000(f)
zinc*	31	73	212	3	722	88	135	1,310	79	1,200	--
aluminum	205	1,900	581	1,610	270	102	253	500	3,450	558	--
barium	7	24	591	21	1,090	37	44	1,370	--	1,420	100,000(f)
boron	--	--	377	--	688	--	89	1,050	--	704	--
calcium	881	198,000	2,660,000	167,000	369,000	8,340	12,000	64,700	16,000	69,400	--
cobalt	--	--	--	--	--	--	18	--	--	--	--

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TABLE III-25 (continued)
SUMMARY OF ANALYTICAL RESULTS FOR SLUDGE SAMPLES
ITD/RCRA SAMPLING PROGRAM

	Plant 12204					Plant 12236			Plant 99999		
	Primary Sludge			Secondary Sludge		Combined Sludge			Secondary Sludge		Regulatory
	Thickened (mg/kg)	Dewatered (mg/kg)	TCLP (µg/ℓ)	Dewatered (mg/kg)	TCLP (µg/ℓ)	Thickened (mg/kg)	Dewatered (mg/kg)	TCLP (µg/ℓ)	Dewatered (mg/kg)	TCLP (µg/ℓ)	Levels (µg/ℓ)
iron	288	850	--	753	521	92,900	18,800	119,000	1,050	829	--
magnesium	377	1,040	--	923	5,860	726	1,170	3,840	1,680	6,510	--
manganese	18	40	--	38	357	365	665	1,940	22	93	--
sodium	435	413	6,700	653	1,380,000	23,500	5,760	1,430,000	5,490	1,560,00	--
tin	5	10	--	7	--	60	16	--	--	109	--
titanium	7	61	--	24	--	72	107	--	--	--	--
vanadium	3	8	--	3	--	77	120	--	--	--	--
Miscellaneous Pollutants											
cyanide, total*	--	4.5	N/A	--	N/A	5.0	6.9	N/A	14	N/A	--
Classical Pollutants											
ammonia, as N	4,600	940	N/A	4,600	N/A	9,300	5,000	N/A	6,300	N/A	--
nitrate-nitrite, as N	1.1	--	N/A	3.4	N/A	4.5	1.1	N/A	33	N/A	--
nitrogen, kjeldahl, total	4,300	14,000	N/A	7,000	N/A	28,000**	73,000	N/A	100,000	N/A	--
flash point (°C)	N/A	52	N/A	37	N/A	40	35	N/A	60	N/A	<60°C(f)
pH	7.6	12.8	N/A	7.5	N/A	8.0	7.3	N/A	6.8	N/A	12.5<ph<2(f)
residue, total(%)	11	38	N/A	22	N/A	3.9	22	N/A	6.9	N/A	--
residue, total volatile(%)	46	7.4	N/A	53	N/A	58	63	N/A	86	N/A	--
sulfide, total (Monier-Williams)	640	88	N/A	75	N/A	7,000	6,000	N/A	620	N/A	--
corrosivity (mpy)	N/A	<10	N/A	<10	N/A	<10	<10	N/A	<10	N/A	>250(f)

N/A Indicates not analyzed.
** Mean of four replicate analyses; refer to the Laboratory Report of Analysis.
-- Indicates pollutant concentration below detection limit.
(f) Final rules for EP Toxicity Characteristic, see 40 CFR 261 Subpart C.
(p) Proposed rules for Toxicity Characteristic, see 51 FR 21648.

IV. TECHNICAL CONTROL AND TREATMENT TECHNOLOGY

A. INTRODUCTION

As indicated in Section III, VOCs are the major unregulated priority and hazardous nonconventional pollutants being discharged by the pharmaceutical manufacturing industry. For the sake of brevity, discussions in this section are limited to those technologies currently used or available to remove or reduce VOCs discharged in the industry wastewater. Technologies currently used or available to remove or reduce other wastewater pollutants generated by this industry are discussed in Section VII of the 1983 Final Development Document.(4)

Many possible combinations of in-plant source controls, treatment technologies, and EOP treatment systems are capable of reducing VOC pollutant discharges. However, each plant must make the final decision concerning the specific combination of pollution control measures best suited to its particular situation.

The treatment technologies currently in-place at plants in the pharmaceutical industry, as reported in 308 responses, are listed in Appendix L of the Proposed Development Document.(5) The technologies described herein are those which can reduce the discharge of volatile pollutants into navigable waters or POTWs. They are divided into two broad classes: in-plant and EOP technologies.

Since the ultimate receiving point of a plant's wastewater (e.g., POTW vs. stream, river, or lake) can be critical in determining the overall treatment effort required, information on ultimate discharge is also presented in this section.

B. IN-PLANT SOURCE CONTROL

The intent of in-plant source control is to reduce or eliminate hydraulic and/or pollutant loads generated by specific sources within the overall manufacturing process. By implementing controls at the source, the impact on and requirements of subsequent downstream treatment systems can be minimized.

The overall planning and plant design criteria of many newer pharmaceutical manufacturing plants include the reduction of water use and subsequent minimization of contamination. Existing plants have also made improvements to provide better control of manufacturing processes and other activities, resulting in environmental benefits. Examples of in-plant source controls effective in reducing volatile organic pollutant loads are as follows:

- Processes have been reviewed and revised to reduce the number of toxic VOCs used. Less toxic non-priority pollutants have been substituted for some of the more toxic priority pollutants (e.g., benzene).

- The recovery of waste solvents used in manufacturing processes is a common practice among plants. However, to further reduce the amount of waste solvent discharge, plants have instituted measures such as: (1) incineration of solvents that cannot be recovered economically, (2) incineration of "bottoms" from solvent recovery units, and (3) design and construction of solvent recovery columns that operate beyond the point at which it is no longer economically feasible to recover solvent(s).

- Spill prevention is recognized in the industry as a critical aspect of pollution control. In addition to careful management of materials and methods, preventive steps such as impoundment basins, dikes, and diversion structures are used in many cases.

C. IN-PLANT TREATMENT

Besides implementing source controls to reduce or eliminate the waste loads generated within the manufacturing process, plants may also use in-plant treatment directed at removing certain pollutants before they are combined with the plants overall wastewater. In-plant treatment processes are appropriate for treatment of wastewater from particular production processes or stage within the plant itself. Although in-plant technologies can remove a variety of pollutants, they are principally applied for the treatment of toxic or priority pollutants.

This concept of in-plant treatment of a segregated stream is of major importance. First, treatment technologies can be directed specifically toward a particular pollutant or a group of pollutants with similar physical chemical properties. Since wastewater treatment and pollutant removal costs are strongly influenced by the volume of water to be treated, the costs involved in treating a segregated stream are often considerably less than they would be in treating combined wastewater. In-plant stream segregation and treatment also can remove substances which may interfere with end-of-pipe treatment, (e.g., biorefractive organics can be removed prior to biological treatment.

The 308 Portfolio data base is the principal source of information relating to the use of in-plant treatment in the pharmaceutical industry. Most of this information came from the Supplemental 308 Portfolio responses. In addition, while not specifically requested in the 308 Portfolio, some in-plant treatment information was obtained from the original 308 Portfolio plants. It was gathered in three ways: (1) some plants provided "additional" data or comments relative to in-plant treatment on the questionnaire; (2) a small amount of information was gathered by direct contact with plant personnel; and (3) the wastewater sampling programs discussed in Section III identified the use of a few in-plant technologies. Some information on in-plant steam-stripping was also obtained

following proposal; as a result of the EPA's efforts to locate an appropriate plant at which to evaluate the performance of steam-stripping technology, and as a result of responses obtained from a post-proposal 308 Questionnaire concerning the discharge of toxic VOCs by indirect-discharging pharmaceutical plants. The responses to the 308 Questionnaire will be discussed later in this section.

1. Solvent Recovery and Removal

Solvents are used extensively in the pharmaceutical manufacturing industry. Because such materials are expensive, most manufacturers try to recover and purify them for reuse whenever possible. Reuse of recovered solvents in the pharmaceutical manufacturing process is quite limited, however, because of FDA constraints on purity requirements for solvents (and other chemicals) used in process. Solvent recovery operations typically use techniques such as decontamination, evaporation, distillation, and extraction. The feasibility and extent of recovery and purification are governed largely by the quantities involved, and by the complexity of solvent mixtures to be separated. If recovery is not economically practicable, the used solvents may have to be disposed of by means of incineration, landfilling, deep-well injection, or contract disposal. It should be noted that hazardous wastes can only be landfilled at approval RCRA landfills.

Even when an effort is made to recover solvents, some wastewater contamination can be expected. Removal of small quantities of organic solvents from the segregated wastewater can be accomplished by techniques such as steam-stripping or carbon adsorption. Further removal of solvents from combined EOP wastewater may result from biodegradation or air stripping during biological treatment or from surface evaporation in the treatment system.

2. Steam-stripping

a. Introduction. Steam-stripping is the transfer of the volatile constituents of wastewater to the vapor phase, which occurs when steam is passed through a preheated wastewater. Extremely volatile compounds can be steam-stripped from wastewater in flash tanks, which essentially provide one stage of liquid-vapor contact. More difficult separations are conducted in columns filled with packing materials, which provide large surface areas for liquid-vapor contact. Conventional fractionating columns, which contain a series of liquid-vapor contact stages, are used for the most difficult separations. Flash tanks, packed towers, and plate columns are used extensively in the chemical process industries; their designs are discussed in chemical engineering textbooks.(11, 12, 13) Hwang and Fahrenthold considered the thermodynamic aspects of steam-stripping organic priority pollutants from wastewater.(14) The authors predict the effluent concentrations theoretically achievable by steam-stripping and the actual number of liquid-vapor contact stages required.

Recently, EPA promulgated a series of steam-stripper based regulations for the Organic Chemicals, Plastics, and Synthetic Fibers Industry (52 FR 42522). The long-term average effluent limitations for most of the pollutants are below 100 ppb. These priority volatile limitations were based on actual performance data from 16 different steam strippers in-place in the OCPSF Industry. Steam-stripping was also demonstrated to be a reliable technology for the removal of methylene chloride and toluene from pharmaceutical wastewater. Section VIII of the 1983 Final Development Document presents suggested limits for these four pollutants based on the performance of wastewater steam-strippers at a pharmaceutical plant. Appendix A of the 1983 Final Development Document presents model costs for the installation of steam-strippers at pharmaceutical plants. Steam stripping operations at Plant 12003 are discussed following the general discussion of steam-stripping.

b. General. In a steam-stripper, the components of wastewater are separated by partial vaporization. When contacted with steam, the VOCs in the wastewater are driven into the vapor phase. The extent of separation is governed by physical properties of the VOCs being stripped, the temperature and pressure at which the stripper is operated, and the arrangement and type of equipment used.

A column used to steam-strip solvents from wastewater is shown in Figure IV-1. Solvent-contaminated process wastewater and condensed overhead vapors from the stripper are allowed to accumulate in a gravity-phase separation tank. When the equilibrium solubility of the solvents in water is reached, the difference between specific gravities of the water and solvents results in the formation of two immiscible liquid layers. One layer contains the immiscible solvents; the other layer is an aqueous solution that is saturated with solvents. The solvent layer is pumped to storage. The composition of the recovered solvent and economic factors will determine whether the solvent is reused within the plant, disposed of, used as incinerator fuel, or sold to other industrial users or a solvent reclamation facility.

The aqueous layer from the gravity-phase separation tank is pumped through a preheater where the temperature is raised by heat exchange with the stripper effluent. If the feed contains high concentrations of suspended solids, a filter can be installed prior to the preheater to prevent fouling in the preheater and the column.

After preheating, the solvent-saturated water is introduced at the top or near the middle of the column, and flows by gravity through the stripper. The hot effluent, which is discharged at the bottom of the stripper, is used as a heating medium in the feed preheater. Steam is injected through a sparger and rises countercurrent to the flow of water.The solvent-laden overhead vapors are condensed, and the organic and aqueous layers are allowed to separate by gravity

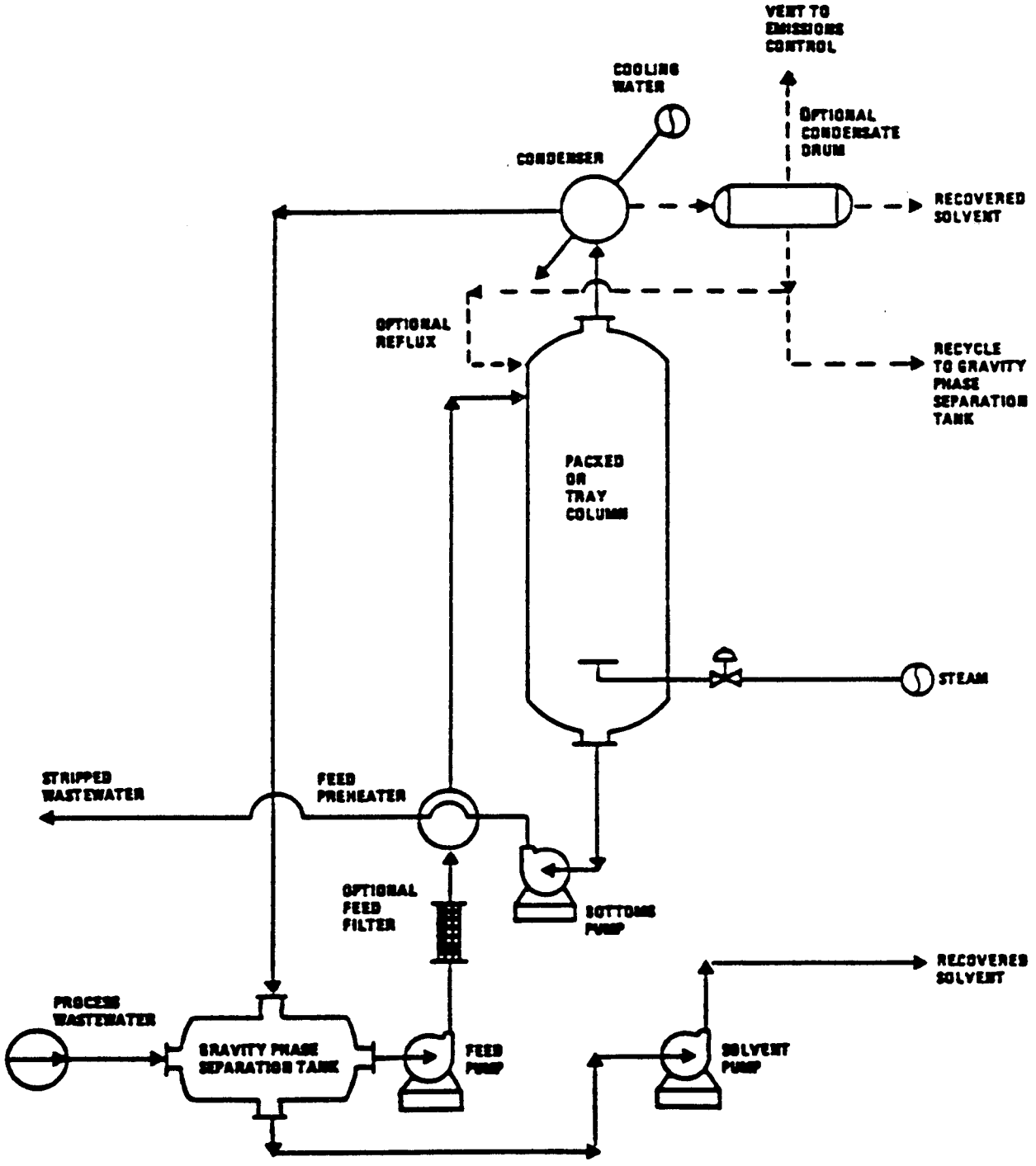

FIGURE IV-1 TYPICAL EQUIPMENT FOR STEAM STRIPPING SOLVENTS FROM WASTEWATER.

in the condensate drum. The solvent can be recovered by decanting the immiscible liquid layers, or by recycling the condensed vapors directly to the gravity-phase separation tank. This practice is particularly advantageous in cases where the wastewater to be steam-stripped contains low concentrations of the solvent to be recovered. As the condensate mixes with the wastewater already in the tank, the solvent concentration increases to the point where a two-phase mixture is formed. The aqueous phase, which is fed to the column, will be saturated with solvent. Steam strippers can be operated to achieve maximum efficiency when the feed is saturated with the solvent to be recovered.

In certain situations, reflux may be required to produce overhead vapors which, when condensed, will separate into immiscible liquid layers. Initially, the condensate is allowed to accumulate in a condensate drum. When the solvent concentration exceeds the water solubility limit, two liquid layers form. The solvent-rich layer is pumped to storage. A portion of the solvent-saturated aqueous layer is returned to the column (i.e., refluxed), and the remainder is recycled to the gravity-phase separation tank. The reflux is introduced at a position above the point where the feed enters the column.

At plants where steam-pressure fluctuations can occur, automatic feedback controllers are commonly used to maintain the desired solvent concentrations in the stripper bottoms and overhead vapors. A detailed discussion of the use of automatic feedback controllers for this purpose is included in the 4th Edition of the Chemical Engineer's Handbook.(15)

Information gathered by EPA indicates that steam-stripping is used to remove organic solvents and other pollutants from wastewater discharges at a minimum of six pharmaceutical plants, and that steam-stripping is also used to treat similar wastewater in other industries. Data on the removal of toxic, volatile organic pollutants in steam-strippers at plants where pesticides and organic chemicals are manufactured are presented in the " Proposed Development Document for Effluent Guidelines Limitations and Standards for the Pesticide Manufacturing Point Source Category" . (16)

The following additional comments are cited from the proposed development document for the organic chemicals and plastics and synthetic fibers point source category: organic steam-stripping may be used in a binary distillation, and is also amenable to multicomponent streams; materials commonly encountered (e.g., methylene chloride, toluene, acetone, diethyl ether, and chloroform) have moderate to high vapor pressure and k-values, and are thus easily separated from water solutions or mixtures.(17)

Actual column efficiencies are critical parameters, as they are used to predict the number of trays required for a column, or the

packing depth for a packed column. For methylene chloride with a saturated inlet concentration and less than 50 ppb outlet concentration, eight trays would theoretically give 100 percent efficiency.

In summary, steam-stripping columns work effectively on most solvents encountered in the pharmaceutical industry. The ultimate degree of separation or removal can be theoretically predicted, as can the cut-off concentration and associated economics (cost of recovery versus solvent value).

Substantial plant operating data (Table IV-1) are also presented showing actual tower heights, diameters, feed rates, and inlet/outlet concentrations for both single solvent and solvent mixtures.

Further reduction of solvent losses to plant effluent streams can be obtained by incineration of solvents not economically recovered by stripping, bottoms incineration, ACA, ion-exchange resin adsorption, or liquid/liquid extractions.

Process changes minimizing wash-ups and clean-ups of process equipment, continuous versus batch production scheduling, and improved solvent handling procedures can significantly reduce solvent losses.

Typical steam-stripping column design criteria follow:

STEAM-STRIPPING

FUNCTION:	Separation of specific dissolved organics from wastewater
PARAMETERS AFFECTED:	Concentration of organics, temperature
EFFECTIVENESS:	Removal to achievable outlet concentration, usually 50 ppb
APPLICATION LIMITS:	TSS: 50 mg/l Oil: 100 mg/l
DESIGN BASIS:	Design flow = 120 percent of the average flow Maximum number of trays = 22 Maximum column diameter = 6 feet Tray spacing = 2.5 feet Organic concentration: No higher than its solubility at ambient conditions
TREATABILITY FACTOR:	Pollutant molecular weight Overall column efficiency Pollutant latent heat of vaporization Achievable effluent concentration (each pollutant)

TABLE IV-1

INDUSTRIAL STEAM-STRIPPERS

Column Type	Height (feet)	Diameter (feet)	Flow Rates (lb/hr) Feed	Flow Rates (lb/hr) Bottoms	Inlet Concentration	Outlet Concentration
Packed*	75.42	3	17,500	1,200	2.63% Aniline	<0.001% Aniline
Trays*	52	3.5	6,960	5,789	5.51% TOC 7.18% Aniline 0.79% Benzene	0.042% TOC 0.03% Aniline 0.02% Benzene
Packed*	33.83	2.5	2,375	5,750	5% Aniline	>0.0005% Aniline
Trays*	80	6.5	70,000	99,750	NA	NA
Packed	54	2.5	33,750	34,300	0.52% Nitrobenzene	0.05% Nitrobenzene
Trays*	38	6	40,000- 90,000	13,900- 31,700	NA	NA
Packed*	36.8	2	7,500	8,200	4,980 ppm TOC 0.18 ppm Methylene chloride 1.05 ppm Methyl chloride 0.001 ppm Phenols	2,360 ppm TOC 0.001 ppm Methylene chloride 0.0018 ppm Methyl chloride 0.0065 ppm Phenols
Trays*	54.5	5.5-7.0	100,080	116,600	778 ppm Sulfide 833 ppm Ammonia 510 ppm Phenols	"Nil" Sulfide 36 ppm Ammonia 284 ppm Phenols
Trays	27.42	4.5-3	90	5,000	0.3% Methylene chloride	0.03% Methylene chloride
Packed*	42	3.0	25,931	23,154	1.07% Aniline 0.019% Methanol	0.009% Aniline 0.01-0.02% TOC

TABLE IV-1 (continued)

INDUSTRIAL STEAM-STRIPPERS

Column Type	Height (feet)	Diameter (feet)	Flow Rates (lb/hr) Feed	Flow Rates (lb/hr) Bottoms	Inlet Concentration	Outlet Concentration
Packed	NA	2.5	16,886	15,886	0.697% TOC 1.88% BOD 0.75% Aniline 0.10% Methanol	0.01-0.02% TOC 0.23% BOD 0.02% Aniline
Trays and Packed*	30.33	1.66-3.25	3,958	3,916	2.3% TOC 2.98% Aniline	0.077% TOC 0.076% Aniline
Packed*	22	1	3,100	3,387	1.35% DIPA 7.26% Salts	0.03% DIPA 6.64% Salts
Packed	15	1	2,746	3,108	0.91% EDC 4.0% NaCl	3.54% NaCl
Packed*	15	2.0	28,600	29,067	0.79% EDC 1.04% HCl	1.025% HCl
Packed*	26	4	43,150	42,870	9,400 ppm EDC	85 ppm EDC 15 ppm VCM
Trays	(not given)	3.5	24,520	25,329	0.0595% TOC 0.076% BOD 0.05% NHs 0.256% Sulfides	0.034% TOC 0.05% BOD 0.012% NHs 0.0037% Sulfides
Packed*	8	0.5	1,611	1,603	6,828 ppm Benzothiazole 620 ppm Aniline	<60 ppm Benzothiazole <60 ppm Aniline
Packed	10.5	0.33	253	254	198 ppm of H_2S Trace-CS_2	Trace H_2S and CS_2

TABLE IV-1 (continued)

INDUSTRIAL STEAM-STRIPPERS

Column Type	Height (feet)	Diameter (feet)	Flow Rates (lb/hr) Feed	Flow Rates (lb/hr) Bottoms	Inlet Concentration	Outlet Concentration
Trays	44	3	28,579	28,906	35 ppm Benzene 4,220 ppm MNB 12,440 ppm Na Salts	0 ppm Benzene 800 ppm MNB 12,300 ppm Na Salts
Trays*	24.83	2.5	41,897	41,669	1% Methylene chloride 0.13% Chlorobenzene 0.00001% Octa-decylamine 5.22% NaCl	0.015% Methylene chloride 0.0025% Chloro-benzene 5.59% NaCl
Trays*	30	2.5	57,000	55,961	0.35% TOC 1.66% Methylene chloride 0.091% Chlorobenzene	0.008% TOC 0.009% Methylene chloride 0.0007% Chloro-benzene
Packed*	17	1.5	0-5,000	0-5,000	800-1,000 ppm Vinyl chloride	<10 ppm Vinyl chloride
Packed	42	3.5	119,000	121,000	0.197% TOC 0.158% BOD 0.011% Vinyl Chloride 0.56% Dichloroethane 0.172% Other Organic chlorides	0.095% TOC 0.112% BOD <0.0001% Vinyl chloride <0.0002% Dichloro-ethane 0.017% Other Organic Chlorides

TABLE IV-1 (continued)

INDUSTRIAL STEAM-STRIPPERS

Column Type	Height (feet)	Diameter (feet)	Flow Rates (lb/hr) Feed	Flow Rates (lb/hr) Bottoms	Inlet Concentration	Outlet Concentration
Packed	28	3.5	112,500	115,000	0.32% TOC 0.004% Vinyl Chloride 0.56% Dichloroethane	0.07% TOC <0.0005% Vinyl chloride 0.021% Dichloro-ethane
Trays*	53	4	60,000	NA	3.3 ppm O/G 1.59 ppm Phenol 750-1,000 ppm TOC <10-1,000 ppm BOD	2.4 ppm O/G 1.99 ppm Phenol 10-100 ppm TOC 40-300 ppm BOD
Trays*	35	4	52,700	51,533	2% "H.C." "(hydrocarbon?)"	50-260 ppm H.C.

* With recycle.

	Steam requirement (each pollutant) Vapor-liquid equilibrium ratio Activity coefficient (deviation from ideal-solution behavior)
COST PARAMETER:	Diameter of the column
COST CURVE SCALE FACTOR:	Number of columns For two or more operating columns (plus a spare), multiply by (number of columns/2)$^{0.8}$ Number of trays
RESIDUES:	Distillate is decanted; water phase is returned to column; organic phase is recovered or incinerated.
MAJOR EQUIPMENT	Feed tank, carbon steel* Distillation columns with sieve trays, carbon steel* Feed preheater, carbon steel* Condensers, carbon steel* Accumulator/decanter, carbon steel* Organic-phase pumps Water-phase recycle pumps Column feed pumps Bottom pumps

* Stainless steel if feed is corrosive or has high salt levels.

c. Steam-stripper Operations at Plant 12003. Plant 12003 can operate up to eight different steam-strippers to reduce VOC concentrations reaching the plant's sewer system. The strippers are located throughout the plant within production buildings, or at central solvent recovery operations in other buildings. Steam-stripping enables the plant to meet a POTW requirement that the concentration of explosive vapors in the plant sewer pipes does not exceed 40 percent of the lower explosion limit (LEL). The LEL is monitored in each production area with a flame-thermocouple sensor. If the solvent vapor concentration exceeds 30 percent of the LEL, gas samples are automatically taken and analyzed by GC. The stripped wastewater is combined with sanitary and other process wastewater in a pretreatment system, which consists of oil skimming, pH adjustment, and flow equalization.

The recovered solvents from the stripping operations are currently stored for disposal by contract hauling. Plant personnel informed EPA that they were considering using some of the recovered solvents as fuel for an incinerator. EPA representatives visited Plant 12003 during the week of May 23-27, 1983, and sampled the influent and effluent from a packed column stripper and a steam distillation flash tank.

d. Packed Column Steam-stripper. Five days of operating data from a packed column steam-stripper, used to remove methylene chloride from wastewater at Plant 12003, are shown in Table IV-2. In

addition to methylene chloride, analysis by plant personnel confirmed that methanol, diethyl ether, and pyridine were also present in the wastewater. The stripper operates approximately 12 hours a day, five days a week. During periods of low production, the stripper is shut down, and wastewater is allowed to accumulate. When the stripper resumes operation, it operates continuously for several days.

The major portion of the feed to the stripper is wastewater from a batch chemical-synthesis operation. The feed is pumped to the underground settling tank shown in Figure IV-2. In the settling tank, the wastewater separates into two layers: immiscible methylene chloride; and an aqueous solution saturated with methylene chloride which also contains small amounts of methanol, diethyl ether, pyridine, and other solvents listed in Table IV-2 footnotes. The immiscible methylene chloride is pumped off the bottom of the settling tank to a spent-solvent holding tank. The aqueous solution is pumped to the stripper feed tank. The feed rate to the column is controlled by an automatic flow valve on the discharge side of the feed pump.

The wastewater is pumped through an influent filter and a preheater before it enters the top of the column through a liquid distributor, which is a special pipe outlet that serves to uniformly wet the tower packing. The 10-inch-diameter column contains one 19-foot section packed with 1-inch-diameter, stainless steel, pall rings. Steam is injected through a sparger in the bottom of the stripper. The overhead vapors from the stripper are condensed and recycled to the underground settling tank.

Results of five days of sampling are shown in Table IV-2. The average influent concentration of methylene chloride was 8,800 mg/l. The column influent also contains high concentrations of inorganic salts. According to plant personnel, the influent and effluent filters shown in Figure IV-2 were installed to prevent fouling in the feed preheater. The average effluent concentration of methylene chloride was 6.9 mg/ when the column was operated close to the design specifications of 98°C overhead vapor temperature. This corresponds to greater than 99-percent removal of methylene chloride in the packed column stripper. The packed column was seemingly operating under unstable conditions, as indicated by a drop in the temperature of overhead vapors below 85°C, during 10 of the 40 overhead temperature readings taken during sampling.

e. Steam Flash Tank. Five days of operating data from a steam flash tank used to strip toluene from wastewater at Plant 12003 are shown in Table IV-3. In addition to toluene, analysis by plant personnel confirmed that methanol, ethanol, acetone, isopropanol, MEK, and diethyl ether were also present in the wastewater. The flash tank normally operates seven hours a day, five days a week.

TABLE IV-2

METHYLENE CHLORIDE REMOVAL IN PACKED COLUMN STEAM STRIPPER AT PLANT 12003
OPERATING DATA FOR 5/23/83

Sample Number	Feed Temp. (°C)	Overhead Temp. (°C)	Bottoms Temp. (°C)	Feed Rate (gpm)	Stream Rate (lbs/hr)	Methylene Chloride (mg/l)	
						Influent	Effluent
1	87	97	104	9.6	160	NA[1]	0.926
2	86	98	102	8.9	160	NA	5.10
3	86	94	101	9.0	150	NA	4.94
4	86	89	102	9.0	150	NA	3.00
5	85	89	102	9.0	150	NA	1.99
6	85	86	102	9.0	150	NA	5.70
7	85	84	102	9.0	155	NA	22.80[2]
8	84	84	101	9.0	155	NA	38.05[2]
Composite of influent samples 1-8						8,250	NA
Average of all effluent datum points							10.31
Average of effluent datum points obtained under normal operating conditions							3.61

[1] NA means not analyzed.

[2] Effluent concentrations under upset conditions, overhead temperature <85°C.

TABLE IV-2 (continued)

METHYLENE CHLORIDE REMOVAL IN PACKED COLUMN STEAM STRIPPER AT PLANT 12003
OPERATING DATA FOR 5/24/83

Sample Number	Feed Temp. (°C)	Overhead Temp. (°C)	Bottoms Temp. (°C)	Feed Rate (gpm)	Stream Rate (lbs/hr)	Methylene Chloride (mg/l)	
						Influent	Effluent
9	84	87	101	8.7	150	NA[1]	3.90
10	84	89	101	9.0	154	NA	8.36
11	83	86	100	8.9	155	NA	20.60
12	85	90	101	8.9	150	NA	4.07
13	84	89	101	9.0	150	NA	10.70
14	84	86	101	9.0	150	NA	20.30
15	84	87	101	9.0	150	NA	4.80
16	84	85	101	9.0	150	NA	7.87
Composite of influent samples 9-16						225[2]	NA
Average of all effluent datum points							10.08

[1] NA means not analyzed.

[2] This datum point is suspect. Plant 12003 collected duplicate samples and reported an average influent methylene chloride concentration of 10,305 mg/l.

TABLE IV-2 (continued)

METHYLENE CHLORIDE REMOVAL IN PACKED COLUMN STEAM STRIPPER AT PLANT 12003
OPERATING DATA FOR 5/25/83

Sample Number	Feed Temp. (°C)	Overhead Temp. (°C)	Bottoms Temp. (°C)	Feed Rate (gpm)	Stream Rate (lbs/hr)	Methylene Chloride (mg/l)	
						Influent	Effluent
17	85	97	102	8.3	150	NA[1]	1.72
18	85	90	102	9.5	150	NA	1.63
19	85	88	102	8.5	150	NA	3.60
20	85	85	102	8.5	150	NA	14.25
21	85	84	102	8.5	150	NA	39.30[2,3]
22	82	83	100	8.5	150	NA	138.0[2,4]
23	83	83	101	UK[5]	152	NA	110.0[2]
24	83	83	UK	UK	155	NA	60.80[2]
Composite of influent samples 17-24						7,000	NA
Average of all effluent datum points							46.2
Average of effluent datum points obtained under normal operating conditions							5.30

[1] NA means not analyzed.

[2] Effluent concentrations under upset conditions, overhead temperature <85°C.

[3] 0.132 mg/l of 1,1-dichloroethylene was detected in effluent sample number 21.

[4] 0.193 mg/l of 1,1-dichloroethylene and 0.302 mg/l of 1,2-dichloropropene were detected in effluent sample number 22.

[5] UK means unknown.

TABLE IV-2 (continued)

METHYLENE CHLORIDE REMOVAL IN PACKED COLUMN STEAM STRIPPER AT PLANT 12003
OPERATING DATA FOR 5/26/83

Sample Number	Feed Temp. (°C)	Overhead Temp. (°C)	Bottoms Temp. (°C)	Feed Rate (gpm)	Stream Rate (lbs/hr)	Methylene Chloride (mg/l)	
						Influent	Effluent
25	84	89	102	8.3	149	11,200	10.1
26	84	86	101	8.3	149	9,900	22.85[1]
27	83	84	101	8.3	150	9,100	57.50[2]
28	82	83	101	8.3	150	9,400	115.00[2]
29	82	83	101	8.3	152	10,200	59.90[2]
30	81	82	101	8.3	152	11,800	127.00[2]
31	83	93	102	7.3	150	10,000	3.18
32	83	89	102	8.3	155	12,000	3.73
Average of all datum points						10,450	49.9
Average of effluent datum points obtained under normal operating conditions							10.0

[1] 0.211 mg/l of 1,1,1-trichloroethane was detected in effluent sample number 26.

[2] Effluent concentrations under upset conditions, overhead temperature <85°C.

TABLE IV-2 (continued)

METHYLENE CHLORIDE REMOVAL IN PACKED COLUMN STEAM STRIPPER AT PLANT 12003
OPERATING DATA FOR 5/27/83

Sample Number	Feed Temp. (°C)	Overhead Temp. (°C)	Bottoms Temp. (°C)	Feed Rate (gpm)	Stream Rate (lbs/hr)	Methylene Chloride (mg/l)	
						Influent	Effluent
33	85	90	102	8.5	150	NA[1]	7.20
34	85	90	102	8.5	150	NA	4.04
35	85	95	102	8.5	154	NA	4.27
36	84	90	102	8.3	154	NA	1.47
37	84	89	102	8.1	154	NA	1.62
38	84	90	102	8.0	152	NA	2.63
39	84	88	102	8.0	160	NA	7.83
40	84	88	102	8.0	170	NA	15.80
Composite of influent samples 33-40						9,500	NA
Average of all effluent datum points							5.61

[1] NA means not analyzed.

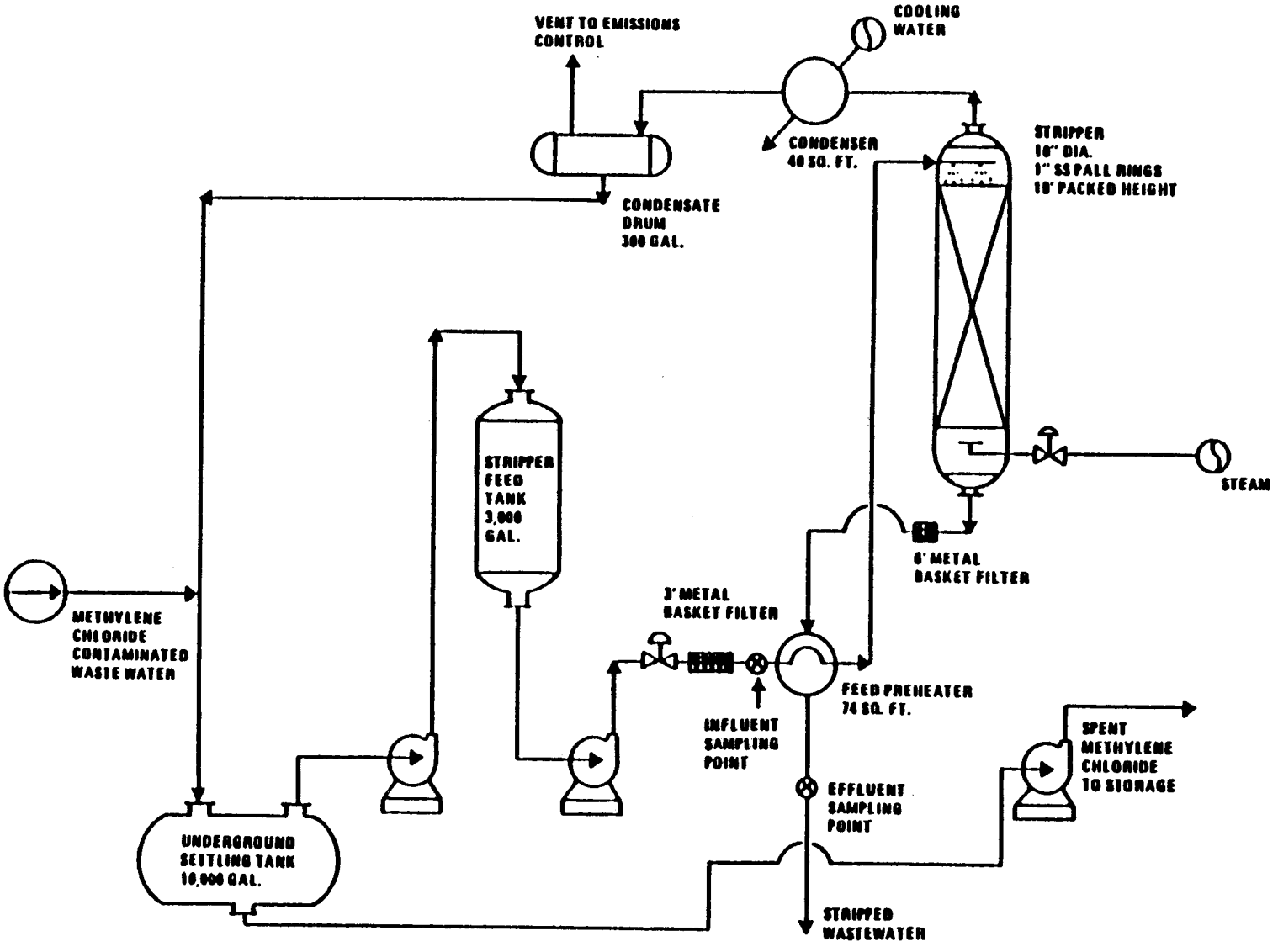

FIGURE IV-2 PACKED COLUMN STEAM STRIPPER AT PLANT 12003.

TABLE IV-3

TOLUENE REMOVAL IN STEAM DISTILLATION FLASH TANK AT PLANT 12003
OPERATING DATA FOR 5/23, 5/24, AND 5/25/83

Date	Sample Number	Toluene (mg/l)		Methylene Chloride (mg/l)		Tank Temp. (°C)	Overhead Temp. (°C)	Bottoms Temp. (°C)	Feed Rate (gmp)
		Influent	Effluent	Influent	Effluent				
5/23/83	1	NA[1]	1.11	NA	ND[2]	99	95	99	12
	2	NA	0.86	NA	0.10	99	98	100	14
	Composite 1 & 2	320.5	NA	7.46	NA				
5/24/83	3	NA	1.46	NA	0.134	99	99	100	18
	4	NA	0.385	NA	0.695	100	98	100	18
	Composite 3 & 4	494.0	NA	7.05	NA				
5/25/83	5	NA	2.590	NA	0.390	100	102	97	9
	6	NA	0.538	NA	0.338	101	103	100	9
	Composite 5 & 6[3]	550.0	NA	6.150	NA				

[1] NA means not analyzed.

[2] ND means not detected.

[3] 2.970 mg/l of chloroform was detected in influent composite sample on 5/25/83.

TABLE IV-3 (continued)

TOLUENE REMOVAL IN STEAM DISTILLATION FLASH TANK AT PLANT 12003
OPERATING DATA FOR 5/26 AND 5/27/83

Date	Sample Number	Toluene (mg/l)		Methylene Chloride (mg/l)		Tank Temp. (°C)	Overhead Temp. (°C)	Bottoms Temp. (°C)	Feed Rate (gmp)
		Influent	Effluent	Influent	Effluent				
5/26/83	7[1,2]	635.0	229.0	31.50	1.740	94	91	95	16
	8[3]	580.0	27.2	5.10	ND[4]	96	98	99	16
5/27/83	9	NA[5]	2.79	NA	1.21	97	97	97	14
	10	NA	3.38	NA	1.59	96	97	98	14
	Composite 9 & 10[6]	4,300	NA	8.570	NA				

[1] 3.15 mg/l of chloroform was detected in influent sample number 7. 1.01 mg/l of chloroform and 0.245 mg/l of benzene were detected in effluent sample number 7.

[2] Effluent concentrations under upset conditions, overhead temperature 91°C.

[3] 0.975 mg/l of 1,1,1-trichloroethane, 2.85 mg/l of chloroform, and 0.915 mg/l of benzene were detected in influent sample number 8.

[4] ND means not detected.

[5] NA means not analyzed.

[6] 9.20 mg/l of methyl chloride was detected in influent composite sample on 5/27/83.

Wastewater from batch pharmaceutical processes, a vacuum pump system, and steam ejectors is accumulated in two 5,000-gallon settling tanks, as shown in Figure IV-3. A connecting line maintains the liquid height at the same level in both tanks. The accumulated wastewater separates into two liquid layers: immiscible toluene, and an aqueous solution of toluene and small amounts of methanol, ethanol, acetone, isopropanol, MEK, diethyl ether, and other solvents listed in Table IV-3 footnotes. The immiscible toluene flows by gravity to a spent-solvent holding tank. The aqueous solution is pumped through two preheaters and enters the top of the 500-gallon flash tank through a spray nozzle. Toluene is stripped from the wastewater by steam, which is injected through a sparger in the bottom of the flash tank. The overhead vapors are partially condensed and introduced to a condensate drum. The liquid condensate is recycled to the settling tanks. Uncondensed vapors from the condensate drum enter a scrubber where they are absorbed in previously uncontaminated cooling water. The scrubber water is recycled to the settling tanks, and the scrubbed vapors are vented to an emissions control system.

As shown in Table IV-3, the concentration of toluene in the influent to the flash tank ranged from 320.5 to 4,300 mg/l. It is suspected that the high influent concentration of 4,300 mg/l on May 27 was caused by a low liquid level in the settling tanks. This probably resulted in a portion of the immiscible toluene being fed to the column, along with the miscible solution of toluene and water. The effluent concentration of toluene ranged from 0.39 to 229.0 mg/l. The high effluent concentration of 229.0 mg/l occurred on May 26 when the tank operated under upset conditions. The temperature of the overhead vapors during the upset period was 91°C; the average temperature of the overhead vapors during the rest of the week was 99°C. The average influent and effluent concentrations for the five-day period were 516 and 4.5 mg/l, respectively, excluding the upset periods. This corresponds to greater than 99 percent removal of toluene in the flash tank.

f. Data Applicability. The vapor-liquid equilibrium relationship of an organic compound in wastewater forms the basis for determining its removability by steam-stripping. The magnitude of the vapor-liquid equilibrium constant serves as a measure of the theoretical removal effectiveness.

The vapor-liquid equilibrium constant, or K-value, is defined as the ratio of the equilibrium mole fraction of an organic compound in the vapor phase, y_i, to its equilibrium mole fraction in the wastewater phase, x_i:

$$K_i = \frac{y_i}{x_i}$$

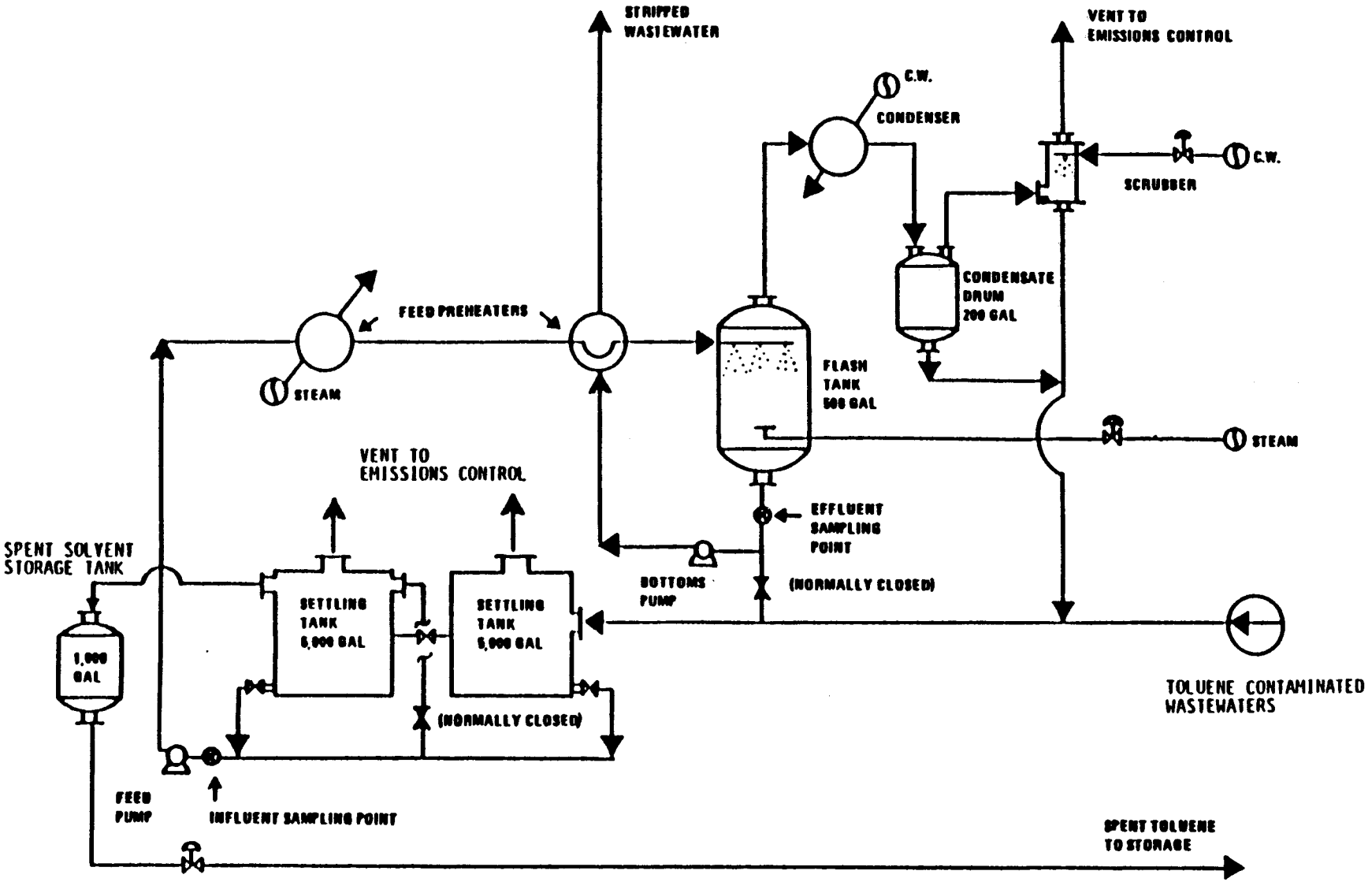

FIGURE IV-3 STEAM DISTILLATION FLASH TANK AT PLANT 12003.

The vapor-liquid equilibrium constant can be calculated from the following equation:

$$K_i = \frac{Y_i P_{io}}{P}$$

where Y_i is the activity coefficient of the organic compound "i" in the wastewater; P_{io} is the vapor pressure of the pure substance at the steam-stripper operating temperature; and P is the total pressure. This expression, which holds for low pressures, is a simplified form of the rigorous thermodynamic equation. Following is a list of vapor-liquid equilibrium constants calculated by Hwang and Fahrenthold for aqueous solutions of toluene, benzene, methylene chloride, and chloroform:(14)

Compound	Average K-Value at 100°C & 1 Atm
Toluene	1,156
Benzene	1,215
Methylene Chloride	941.4
Chloroform	635.5

The suggested limits in Section VIII of the Final Development Document for benzene are based on the performance of the steam distillation flash tank in removing toluene from pharmaceutical process wastewater at Plant 12003. The suggested limits for chloroform are based on the performance of the packed column steam-stripper in removing methylene chloride from pharmaceutical process wastewater at Plant 12003. In both cases, the use of identical limits is justified by these similarities between the vapor-liquid equilibrium constants.

3. Carbon Adsorption

Adsorption is defined as the adhesion of dissolved molecules to the surface of solid bodies with which they are in contact. Two properties make granular activated carbon (GAC) particles effective and economical adsorbents. First, they have a high surface area per unit volume, which results in faster, more complete adsorption. Second, they have a high hardness value, which lends GAC particles to reactivation and repeated use.

The adsorption process typically is preceded by preliminary filtration or clarification to remove insolubles. Next, the wastewater is placed in contact with carbon so adsorption can take place. Normally, two or more beds are used so that adsorption can continue while a depleted bed is reactivated. Reactivation is accomplished by heating the carbon between 870°C and 980°C (1600°F and 1800°F) to volatilize and oxidize the adsorbed contaminants. Oxygen in the furnace is normally controlled at less than 1 percent

to avoid loss of carbon by combustion. Contaminants may be burned in an afterburner.

Carbon adsorption is primarily designed to remove dissolved organic material from wastewater, although it can to some extent remove chromium, mercury, and cyanide. The technical and economic feasibility of ACA technology is discussed in "Treatability of Priority Pollutants in Wastewater by Activated Carbon" (S. T. Hwang and P. Fahrenthold; US EPA, 1979).(14)

The potential use for this technology by the pharmaceutical industry is limited. Concentrations of most toxic pollutants (i.e., metals, VOCs, and cyanide) characteristic of pharmaceutical wastewater are generally reduced more effectively and with less cost by the previously discussed technologies, or through biological treatment, than by ACA. Phenols, the other group of pollutants found in pharmaceutical wastewater, are biodegradable, and their concentrations can be reduced by advanced biological treatment. Carbon adsorption is particularly applicable in situations where organic material in low concentrations, not amenable to treatment by other technologies, must be removed from wastewater.

The equipment necessary for an activated carbon adsorption treatment system consists of a preliminary clarification and/or filtration unit to remove the bulk of suspended solids, two or three columns packed with activated carbon, and pumps and piping. When on-site regeneration is used, a furnace, quench tanks, spent carbon tank, and reactivated carbon tank are generally required. Contract regeneration at a central location is a frequent commercial practice, particularly if carbon use is less than 1,000 lb/day. An example of an ACA unit is shown in Figure IV-4.

Carbon adsorption systems are compact, will tolerate variations in influent concentrations and flow rates, and can be thermally desorbed to recover the carbon for reuse. Economic application of carbon adsorption is limited to the removal of low pollutant concentrations. Competitive adsorption of non-target constituents, as well as blinding by suspended solids, can be a source of interference.

Pilot plant studies recently conducted by EPA evaluated the performance of ACA treatment technologies using actual pharmaceutical plant wastewater to consistently achieve reductions in effluent COD.(18) The two ACA treatment technologies evaluated were (1) PAC enhancement of an activated sludge system; and (2) GAC treatment of plant secondary effluent.
Conclusions from the biological treatment study are as follows:

- Effluent soluble chemical oxygen demand (SCOD) concentrations were significantly reduced by the addition of PAC to the feed to activated sludge treatment.

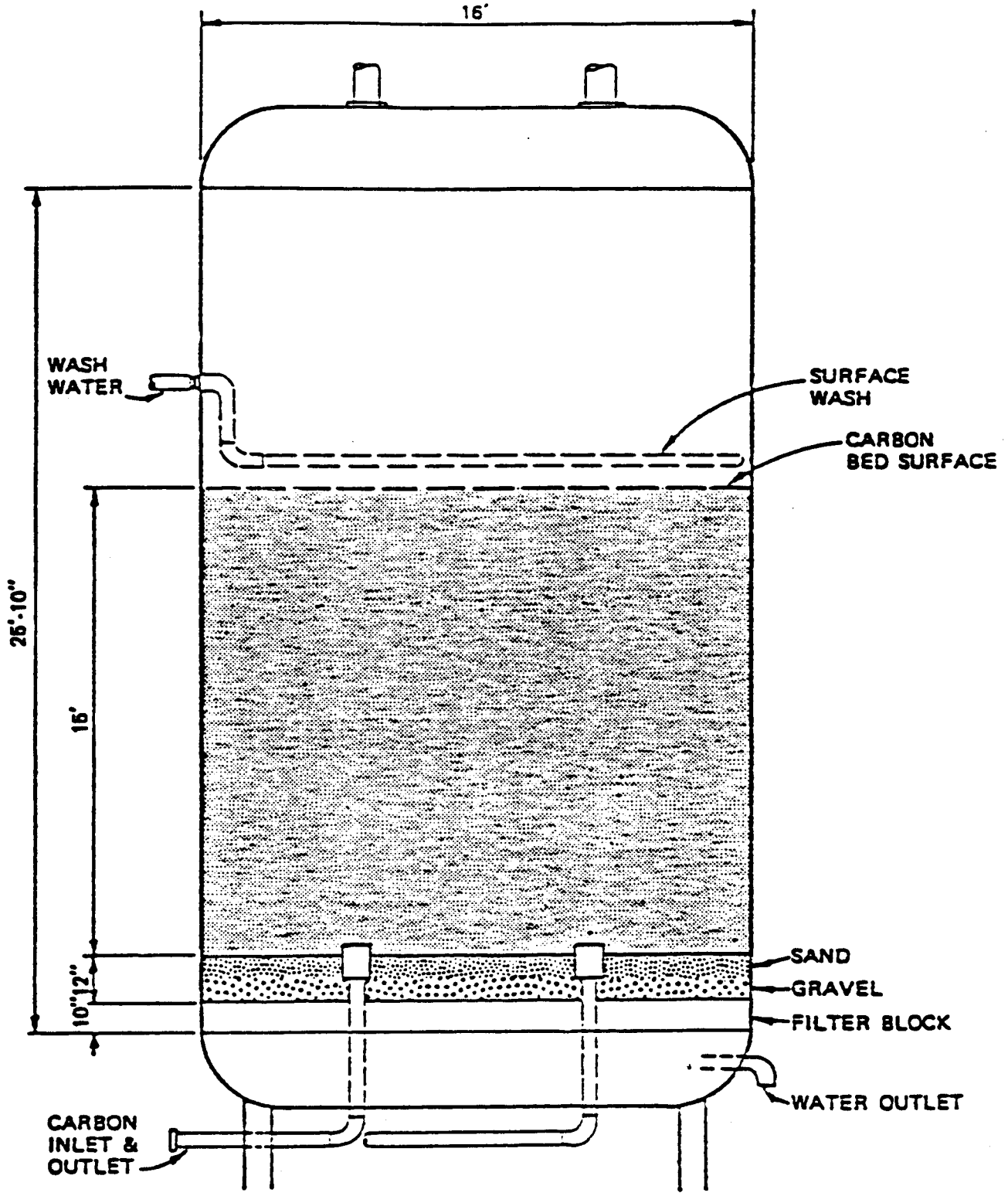

FIGURE IV-4

ACTIVATED CARBON ADSORPTION UNIT

Effluent SCOD concentrations were reduced by 44, 54, 68, and 67 percent of the control plant effluent SCOD concentrations when adding 208, 496, 827, and 1,520 mg/l PAC, respectively. The control pilot plant reduced SCOD concentrations from 8.6 to 10.2 percent of feed TCOD, whereas the PAC unit reduced the SCOD concentrations to 5.6 percent of feed TCOD (208 mg/l PAC) to 2.8 percent (1,520 mg/l PAC).

- o The sludge volume index (SVI) of the mixed liquor solids was improved by the addition of PAC.

- o Denitrification developed in the final clarifier of both units containing PAC, causing some solids to float. Denitrification was not apparent in the control unit.

- o A viscous floating mass of mixed liquor solids (VFMLS) developed in both PAC units near the end of the tests. The VFMLS was very cohesive and difficult to redisperse in water. The VFMLS did not appear in the control unit during these tests. The PAC/activated sludge process cannot be recommended as a reliable treatment process for this wastewater until the cause of the VFMLS is identified and adequate safeguards against its occurrence are demonstrated.

Conclusions from the GAC study are as follows:

- o The combination of biological treatment and GAC could remove 96 percent of the raw waste TCOD. This is 22 percent above the currently required BPT level of 74 percent removal.

- o Carbon usage was found to be a function of the effluent SCOD concentration. Carbon usage rates determined from the pilot study are summarized in the following table.

Design effluent SCOD, mg/l	300	400	500
Carbon usage, kg/1,000 (lb/1,000 gal)			
Run No. 2	2.6 (21.3)	2.1 (17.5)	1.6(13.6)

- o The removal of specific organics as measured by GC is directly related to the removal of SCOD by GAC treatment.

D. END-OF-PIPE TREATMENT

In-plant treatment processes are used to treat specific pollutants in segregated wastestreams; EOP technologies usually are designed

to treat a number of pollutants in a plant's overall wastewater discharge. The types and/or stages of EOP treatment are primary, biological, and tertiary. Depending on the nature of the pollutants to be removed, and the degree of removal required, various combinations of the available technologies are used.

As in the case of in-plant treatment, the 308 Portfolio data base was the principal source of information for identifying the use of EOP treatment by the pharmaceutical industry. This information was requested in both 308 Portfolio mailings. As a cross-check for accuracy and completeness, the 308 Portfolio responses were compared to information available from the other data bases. Table IV-4 summarizes the EOP technologies identified by the various data bases, along with the number of plants that use each process.

1. Primary Treatment

Primary treatment, a form of physical/chemical treatment, refers to those processes that are nonbiological in nature. Primary treatment involves (1) the screening of the influent stream to remove large solids, and (2) gravity separation to remove settleable solids and floating materials. Commonly used primary treatment technologies in the pharmaceutical industry are coarse solids removal, primary sedimentation, primary chemical flocculation/clarification, and dissolved air flotation.

In a 1984 field study of a wastewater treatment system at an organic chemicals facility, 10-15 percent of the influent toluene volatilized in the primary system.

2. Biological Treatment

Biological treatment is the principal method by which many pharmaceutical manufacturing plants are now meeting existing BPT regulations. Although it is discussed as a single EOP treatment alternative, biological treatment actually encompasses a variety of specific technologies (e.g., aerated lagoons, activated sludge, trickling filters, and rotating biological contactors [RBCs]). Because numerous publications are available describing all aspects of the operations (i.e., advantages, limitations, and other pertinent facts), these specific treatment processes will be discussed in only moderate detail herein. Although each process has unique characteristics, all are based on one fundamental principle: the reliance on aerobic and/or anaerobic biological microorganisms for the removal of oxygen-demanding compounds.

Although the primary purpose of biological treatment is usually to reduce the overall oxygen demand of wastewater, biological treatment can also remove some specific toxic compounds. The major mechanisms for removal of toxic chemicals are as follows:

TABLE IV-4

SUMMARY OF EOP TREATMENT PROCESSES
(DATA BASE: 308)

EOP Technology	Number of Plants
Equalization	62
Neutralization	80
Primary Treatment	
Coarse Settleable Solids Removal	41
Primary Sedimentation	37
Primary Chemical Flocculation/Clarification	12
Dissolved Air Flotation	3
Biological Treatment	
Activated Sludge	52
o Pure Oxygen	1
o Powered Activated Carbon	2
Trickling Filter	9
Aerated Lagoon	23
Waste Stabilization Pond	9
Rotating Biological Contactor	1
Other Biological Treatment	2
Physical/Chemical Treatment	
Thermal Oxidation	3
Evaporation	6
Additional Treatment	
Polishing Ponds	10
Filtration	17
o Multimedia	7
o Activated Carbon	4
o Sand	5
Other Polishing	17
o Secondary Chemical Flocculation/Clarification	5
o Secondary Neutralization	5
o Chlorination	11

- o Biodegradation of the chemical into simpler compounds. In some cases, the compounds produced may be more toxic than the chemicals degraded. Chlorinated compounds are often difficult to degrade.

- o Adsorption of the chemical onto biological solids. Heavy metals and large hydrophobic organic compounds are most readily adsorbed. The sludge containing these toxic solids must be properly treated prior to disposal.

- o Air-stripping to the atmosphere of VOCs in those processes that include aeration (e.g., activated sludge). High concentrations of TVOs in the wastewater may generate air pollution problems near the treatment facility.

The fate of pollutants in biological treatment systems depends on a number of complex and interrelated factors that include the design of the treatment system, its operation and maintenance, the physical/chemical properties of the individual pollutants, and the physical/chemical properties of the wastestream as a whole. These factors are often highly site specific.

None the less, in open biological treatment systems, volatilization is expected to predominate over biodegradation and adsorption for many of the ITD-listed VOCs. In support of this hypothesis, Petrasek reported a strong correlation between the Henry's law constant and the fraction of priority pollutants found in the activated sludge off-gass.(18)

Henry's law constant is the relative equilibrium concentration of a compound in air and water at a constant temperature and is defined by the following equation:

$$K = \frac{P}{S}$$

where

K = Henry's law constant, m^3x atmosphere $mole^{-1}$
P = compounds vapor pressure in atmospheres
S = compounds solubility in water in moles per cubic meter

The constant is an expression of the equilibrium distribution of a compound between air and water. The constant indicates qualitatively the volatility of a compound and is frequently used in equations that attempt to predict "stripping" of a compound from aqueous solution. Increasing values of the constant favor volatilization as a fate mechanism and indicate amenability to steam- or air-stripping. Henry's law constants for selected VOCs are shown in Table IV-5. The toxic compounds frequently present in industrial wastes can inhibit or upset biological processes. Acclimation, however, can produce strains of organisms which are

TABLE IV-5
HENRY'S LAW CONSTANTS FOR SELECTED
VOLATILE ORGANIC COMPOUNDS

VOC	Henry's Law Constants ($atmos.m^3\ mole^{-1}$)	
acrolein	0.000077	(15°C)
acrylonitrile	0.0000666	(15°C)
benzene	0.00555	(25°C)
bromomethane	0.22	(25°C)
chlorobenzene	0.00393	(25°C)
chloroform	0.00339	(25°C)
chloromethane	0.0368	(25°C)
cyclohexane	0.16	(25°C)
1,1-dichloroethane	0.00545	(25°C)
1,2-dichloroethane	0.00110	(25°C)
1,1-dichloroethene	0.0150	(25°C)
trans-1,2-dichloroethene	0.00532	(25°C)
diethylamine	0.00011	(50°C)
ethyl benzene	0.00644	(25°C)
methylene chloride	0.00319	(25°C)
methyl mercaptan	0.00385	(25°C)
tetrachloroethene	0.0287	(25°C)
tetrachloromethane	0.0302	(25°C)
toluene	0.00593	(25°C)
trichloroethene	0.0117	(25°C)
1,1,1-trichloroethane	0.00492	(25°C)
vinly acetate	0.000594	(25°C)
vinyl chloride	0.036	(25°C)
xylenes	0.00612	(25°C)

Source: Reference No. 19.

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tolerant to normally toxic substances. Nonetheless, once the specialized strain is established, major changes in wastewater composition or concentration can kill the acclimated organisms and cause breakdown or upsets in the treatment process. Reestablishment of a suitable microbial population can require months.

An aerated lagoon is one example of a treatment facility that uses aerobic biological processes. It is essentially a stabilization basin to which air is added, either through diffusion or mechanical agitation. The air provides the oxygen required for aerobic biodegradation of the organic waste. If properly designed, the air addition will provide sufficient mixing to maintain the biological solids in suspension so they can be removed in a secondary sedimentation tank. After settling, sludge may be recycled to the head of the lagoon to ensure the presence of a properly acclimated seed. When operated in this manner, the aerated lagoon is analogous to the activated sludge process. The viable biological solids level in an aerated lagoon is low when compared to that of an activated sludge unit. The aerated lagoon relies primarily on detention time for the breakdown and removal of organic matter; aeration periods of three to eight days or more are common.

The activated sludge process is also an aerobic biological process. The basic process components include an aerated biological reactor, a clarifier for separation of biomass, and a piping arrangement to return separated biomass to the biological reactor. The aeration requirements are similar to those of an aerated lagoon, in that aeration provides the necessary oxygen for aerobic biodegradation and mixing to maintain the biological solids in suspension. The available activated sludge processes that are used in the treatment of wastewater include conventional, step, tapered, modified, contact-stabilization, complete-mix, and extended aeration.

A trickling filter is a fixed-growth biological system where a thin-film biological slime develops and coats the surfaces of the supporting medium as wastewater makes contact. The film consists primarily of bacteria, protozoa, and fungi that feed on the waste. Organic matter and dissolved oxygen are extracted, and the metabolic end products are released. Although very thin, the biological slime layer is anaerobic at the bottom, resulting in the generation of hydrogen sulfide, methane, and organic acids. These materials cause the slime to periodically separate (slough off) from the supporting medium and be carried through the system with the hydraulic flow. The sloughed biomass must be removed in a clarifier.

Trickling filters are classified by hydraulic or organic loading as "low rate" or "high rate." Low-rate filters generally have a hydraulic loading rate of 1 to 4 million gallons/acre/day (or an organic loading rate of 300 to 1,000 lbs. BOD_5/acre-feet/day), a depth of 6 to 10 feet, and no recirculation. High-rate filters

have a hydraulic loading rate of 10 to 40 million gallons/acre/day, an organic loading rate of 1,000 to 5,000 lbs. BOD_5/acre-feet/day, a depth of 3 to 10 feet, and a recirculation rate of 0.5 to 4.0. High-rate filters can be single- or two-stage. The medium material used in trickling filters must be strong and durable. The most suitable medium in both the low and high-rate filters is crushed stone or gravel graded to a uniform size.

The RBC process consists of a series of disks constructed of corrugated plastic plates and mounted on a horizontal shaft. These disks are placed in a tank with a contour bottom and immersed to approximately 40 percent of the diameter. The disks rotate as wastewater passes through the tank, and a fixed-film biological growth, similar to that on trickling filter media, adheres to the surface. Alternating exposure to the wastewater and the oxygen in the air results in biological oxidation of the organics in the wastes. Biomass sloughs off (as in the trickling filter) and is carried out in the effluent for gravity separation. Direct recirculation is not generally practiced with rotating biological disks.

Three other biological treatment techniques not specifically mentioned in this section use either aerobic or anaerobic biodegradation or both: stabilization ponds, anaerobic lagoons, and faculative lagoons. In faculative lagoons, the bacterial reactions include both aerobic and anaerobic decomposition.

Besides the direct utilization of these treatment processes, biological treatment also encompasses two other approaches; in this report, they are referred to as biological enhancement and biological augmentation. Generally, these variations are accomplished by: (1) modifications made in the conventional biological treatment itself, or (2) conventional processes combined into a multi-stage system. Examples of biological enhancement are pure oxygen activated sludge and biological treatment with PAC. Biological augmentation could be trickling filter/activated sludge, activated sludge/RBC, aerated lagoon/ polishing pond, or any combination of two or more conventional biological treatment processes.

The differences in performance due to the number of biological treatment stages used rest on the applicability of plug-flow/back-mix effects. A true plug-flow system (e.g., a narrow channel lagoon) approaches equivalence to an infinity of stages if the food/microorganism (F/M) ratio is maintained. This tends to beneficially maximize the availability of nutrients, a function of the concentration of biodegradable pollutants. A fully back-mixed system (as an activated sludge unit tends to be) operates throughout at its exit concentration. It is thus a distinct, finite stage incremental from any stage before or after it.

In practice, these distinctions are not clearcut. Since there is some back-mixing even in a channel lagoon, separations of units or even of cells within one unit may be beneficial. Also, in most mixed systems, the concentration gradient established is sufficient

for some increase in the effective nutrient concentration and, consequently, the optimum microorganism concentration.

In many systems, design factors other than the concentration-induced driving force may overshadow the concentration gradient and prevent simple performance correlation.

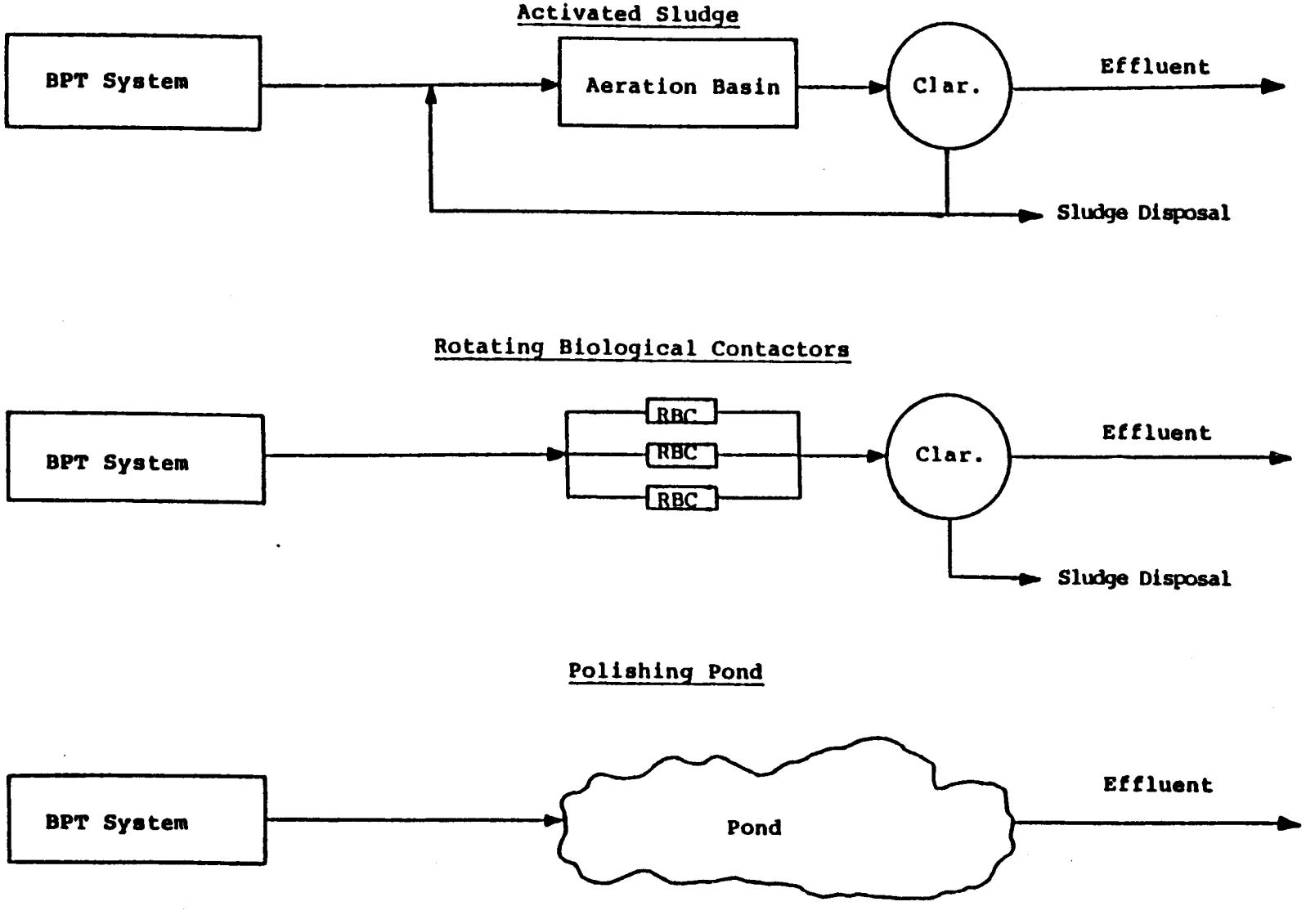
Comprehensive consideration of the criteria affecting bioreaction performance suggests the following to be significant:

- influent concentration of pollutants
- resistive characteristics of the BOD pollutants and the resultant K value (i.e., how easily the BOD is biodegraded)
- presence of potential interfering pollutants (e.g., constituents toxic to the microorganisms)
- bioreaction characteristics and concentration of the microorganisms present
- dissolved oxygen content and distribution at least to the point of adequate O_2 availability
- sludge recycle as it may affect microorganism availability and character, as represented by the F/M ratio
- contact efficiency of pollutants and microorganisms, as may be induced by agitation, flow pattern, and mixed liquor volatile suspended solids (MLVSS)
- availability and balance of nutrients, including nitrogen and phosphate
- required target effluent
- temperature (e.g., seasonal effects)

The proper design of biological systems in addition to developing optimum operating criteria, must also consider how much of the system's potential capacity will be used so that an optimum modification approach will be available. The most economical approach may be simple adjustments of operating variables to fully exploit existing capacity. The adjustments may require minor changes such as increasing agitation, power input, or sludge recycle rate or, at the extreme, the addition of an independently functioning system. In many cases, the optimum upgrade may be a combination of existing component units integrated with balanced new units. This is likely to result in a system complex dictated in part by performance requirements, and in part by equipment already in place. Some examples of typical augmented biological configurations are shown in Figure IV-5.

FIGURE IV-5

EXAMPLES OF AUGMENTED BIOLOGICAL SYSTEMS



Biological treatment systems are mainly intended to reduce the level of the traditional pollutants BOD and COD. However, some priority pollutants may be removed incidentally.

Biological treatment removal efficiency is a function of treatment intensity, detention time, and system characteristics such as bioreaction rate constant, biomass concentration, and biomass contact efficiency. The configuration of the system is important since it affects these factors, but the effectiveness is not necessarily benefitted by splitting the bioreaction into a number of steps. In a plug-flow (i.e., non-backmixed) system, there is a continuation of reaction and little inherent effect of staging as in certain separation techniques and driving force systems. Reaction rate advantages in a back-mixed system may accrue from staging, but these must be evaluated for a specific system in the context of microorganism availability, contact efficiency, and other factors.

Economic concerns often dictate a design that uses (1) one biotechnique in preference to others, (2) more than one technique as the reaction progresses (e.g., activated sludge and trickling filter), or (3) various arrangement configurations. However, these design choices are highly site- and waste-specific, and generalizations should be avoided in the comparison of systems andthe choice of a particular treatment configuration.

3. Pollutant Treatability and/or Removal

Information on the treatability of ITD-listed VOC pollutants was obtained in the recent sampling program conducted at Plants 12236, 99999, and 12204. Influent and effluent streams from each plant's activated sludge wastewater treatment plant were sampled for two consecutive 24-hour periods. The following paragraphs present information on pollutant reduction by comparing the two-day average influent and effluent concentrations. The observations noted are general in nature because the data are from a very short sampling period, which may or may not represent typical treatment plant performance.

a. Plant 12236. Plant 12236 is a direct-discharging facility providing primary and secondary (activated sludge) treatment for its wastewater. The treatment plant appeared well-operated during the recent sampling visit, achieving average effluent BOD_5 and TSS levels of 22 and 26 mg/l, respectively. These effluent levels represent average BOD_5 and TSS reductions of 99 and 86 percent, respectively (Table IV-6).

Effluent wastewater concentrations of VOCs were consistently low (i.e., less than 174 ppb, or at below detectable levels), with the exception of approximately 1 ppm of 2-hexanone for one day (see Table IV-6). Analytical results for the dewatered sludge sample indicate that several pounds of VOCs can leave the plant with the sludge (see Table III-19).

TABLE IV-6

AVERAGE WASTEWATER POLLUTANT LEVELS
ITD/RCRA SAMPLING PROGRAM
PLANT 12236

Compounds	Primary Influent**	Final Effluent**	Percent Removal
Volatile Organics (µg/ℓ)			
carbon tetrachloride*	<10	22	--
methylene chloride*	5,247	92	98
toluene*	<10	10	--
acetone	928	134	86
2-hexanone	<50	562	--
Semivolatile Organics (µg/ℓ)			
None detected			
Metals (µg/ℓ)			
chromium*	22	11	50
nickel*	20	<40	--
zinc*	140	34	76
aluminum	147	<100	TBDL
barium	105	<50	TBDL
boron	108	<100	TBDL
calcium	51,600	57,700	--
iron	145,000	4,890	97
magnesium	1,740	1,390	20
manganese	1,080	239	78
sodium	1,620,000	1,530,000	6
titanium	105	<50	TBDL
vanadium	107	<50	TBDL
Miscellaneous (µg/ℓ)			
cyanide*	nr	27	--
Conventional Pollutants (mg/ℓ)			
BOD_5	1,817	22 (182)***	99
TSS	432	62 (309)***	86
oil and grease	6	19	--
Nonconventional Pollutant (mg/ℓ)			
COD	2,250	390(585)****	83

* Priority pollutant.

** Flow-weighted average of two 24-hour composite samples.

*** BPT annual average effluent levels assuming an annual average influent BOD_5 level of 1,817 mg/ℓ.

**** BPT annual average effluent level assuming an annual average influent COD level of 2,250 mg/ℓ

nr No value reported due to matrix interference.

TBDL To below detection limit.

No information on the removal of semivolatile organic compounds (SVOCs) from wastewater is available, as none were found to be present above the analytical detection limits. However, analytical results for the grab sample of the dewatered sludge indicate that bis(2-chloroethyl)ether and n-octadecane may tend to concentrate in the sludge (see Table III-19).

Reduction of the metals detected at levels significantly above analytical detection limits was very good with the exception of calcium, magnesium, and sodium, which incurred little or no reduction (see Table IV-6).

b. Plant 99999. This plant is an indirect discharger providing activated sludge pretreatment for wastewater. The wastewater treatment plant at this site consists of pH adjustment with lime or H_2SO_4, equalization, and a step-feed activated sludge system followed by degasification and sedimentation. The hydraulic detention of the treatment system (excluding equalization) is approximately 8.5 hours. The low detention time is due primarily to the high recycle rate (5:1). The equalization, aeration, and degassing tanks are covered and the off-gasses are vented to the power boilers. The treatment plant appeared to be operating well during the recent sampling visits; however, treated effluent BOD5 levels were significantly higher than the long-term average levels previously reported for this plant.

	Wastewater Comparison		
	Flow (mgd)	BOD5 (mg/l)	TSS (mg/l)
Combined Influent			
1975-76 Data	0.65	3,000	950
ITD/RCRA Sampling	0.7	2,700	940
Treated Effluent			
1975-76 Data	0.65	120	500
ITD/RCRA Sampling	0.7	365	248

During the sampling program, VOCs were very effectively removed by their activated sludge treatment plant. Based on the two-day averages, VOCs were reduced better than 99 percent, or to below detectable levels (Table IV-7). It is important to note that this plant operates degassing tanks between the aeration basin and secondary clarifiers, which may aid in the air-stripping of these VOCs.

Observed reductions of SVOCs were not as significant as for the VOCs because influent concentrations were generally low (see Table IV-7). The single grab sample of the thickened waste activated

TABLE IV-7

AVERAGE WASTEWATER POLLUTANT LEVELS
ITD/RCRA SAMPLING PROGRAM
PLANT 99999

Compounds	Aeration Influent**	Pretreated Effluent**	Percent Removal
Volatile Organics (µg/ℓ)			
acrylonitrile*	68	<50	TBDL
chloroform*	6,537	25	99.6
ethylbenzene*	330	<10	TBDL
methylene chloride*	8,523	73	99.1
toluene*	4,241	<10	TBDL
acetone	465,130	340	99.9
2-butanone (MEK)	371	<50	TBDL
Semivolatile Organics (µg/ℓ)			
benzidine*	103	160	--
bis(2-ethylhexyl) phthalate*	<10	11	--
2-chloronaphthalene*	38	42	--
4-chloro-3-methylphenol*	74	<10	TBDL
3,3-dichlorobenzidine*	44	<50	--
N-nitrosodi-n-propylamine*	<20	21	--
alpha-terpineol	7	<10	--
diphenyl ether	7	<10	--
2-methylnaphthalene	<10	498	--
n-dodecane	<10	13	--
n-eicosane	103	231	--
n-hexacosane	95	<10	TBDL
p-cresol	9	<10	--
Pesticides/Herbicides (µg/ℓ)			
BHC, alpha*	<4	3.1	--
BHC, beta*	<4	0.66	--
TEPP	2,063	484	77
Metals (µg/ℓ)			
arsenic*	17	12	29
chromium*	27	24	11
copper*	440	43	90
nickel*	50	22	56
selenium*	14	4.2	70
silver*	1.1	<1	TBDL
zinc*	150	40	73
aluminum	2,700	818	70
barium	69	33	52
boron	87	90	--
calcium	165,000	98,500	40
cobalt	2	<4	TBDL
iron	2,350	690	71
magnesium	19,000	17,500	8
manganese	97	43	56
sodium	915,000	715,000	22
titanium	58	100	--
vanadium	8	2	75
Miscellaneous Priority Pollutants (µg/ℓ)			
cyanide*	16	<20	TBDL

TABLE IV-7 (continued)

AVERAGE WASTEWATER POLLUTANT LEVELS
ITD/RCRA SAMPLING PROGRAM
PLANT 99999

Compounds	Aeration Influent**	Final Effluent**	Percent Removal
Conventional Pollutants (mg/ℓ)			
BOD5	2,700	365	86
TSS	940	248	74
oil and grease	47	16	66
Nonconventional Pollutant (mg/ℓ)			
COD	7,200	1,450	80

* Priority pollutant.
** Flow-weighted average of two 24-hour composite samples.

sludge, which may or may not relate to the wastewater treated during the sampling program, indicated that three SVOCs (i.e., 2-chloronaphthalene, 2-methyl naphthalene, and n-eicosane) tended to concentrate in the sludge (see Table III-21).

Metals found at levels significantly above their analytical detection limit were significantly reduced, except for calcium, magnesium, and sodium.

c. Plant 12204. Plant 12204 is an indirect-discharging facility providing activated sludge pretreatment for process wastewater. The wastewater treatment plant at this facility consists of pH adjustment with lime, followed by primary clarification, followed by oxygen-activated sludge treatment system, followed by a final clarifier. Hydraulic detection through the treatment system is estimated to be approximately 19 hours.

The treatment plant appeared to be operating well during the recent sampling visit; however, the treated effluent BOD5 levels were significantly higher than the long-term average levels previously reported for this plant.

Wastewater Comparison

	Flow (mgd)	BOD5 (mg/l)	TSS (mg/l)
Combined Influent			
1975-76 Data	1.2	1,200	2,000
ITD/RCRA Sampling	2.0	1,700	1,500
Treated Effluent			
1975-76 Dattaa	1.2	146	320
ITD/RCRA Sampling	2.0	360	260

During the sampling program, VOCs appeared to be less effectively removed through its pure oxygen-activated sludge treatment system than for the air-activated sludge system at Plants 12236 and 99999 (see Table IV-8). Finding VOCs at ppm levels in the effluent of this pure oxygen-activated sludge system corroborates similar findings by EPA at other systems. The use of a covered and slightly pressurized aeration basin probably eliminates air-stripping as a removal pathway for VOCs. Long-term studies may be warranted to study biodegradation rates within this type of system. Of interest also is that significant quantities of acetone were found in the one-time grab sample of both the primary and secondary sludges (see Table III-18).

Little information on the removal of SVOCs from wastewater is available because only phenol was detected, and it was found at levels slightly above the detection limit. Results of the one-time

TABLE IV-8

AVERAGE WASTEWATER POLLUTANT LEVELS
ITD/RCRA SAMPLING PROGRAM
PLANT 12204

Compounds	Raw Wastewater**	Pretreated Effluent**	Percent Removal
Volatile Organics (µg/ℓ)			
acrolein*			
benzene*	39	<50	TBDL
chloroform	13	16	--
1,1-dichloroethane*	349	57	84
trans-1,2-dichloroethene	<10	16	--
methylene chloride*	<10	13	--
toluene*	4,771	2,705	43
1,1,1-trichloroethane*	2,256	3,952	--
	46	32	30
acetone	93,562	58,314	38
diethyl ether	8,703	7,732	11
vinyl acetate	52	33	37
Semivolatile Organics (µg/ℓ)			
phenol*	<100	59	--
Metals (µg/ℓ)			
cadmium*	2	<5	TBDL
chromium*	14	<10	TBDL
copper*	163	51	69
selenium*	6	5	17
zinc*	294	154	48
aluminum	2,480	1,290	50
barium	127	84	34
calcium	273,000	254,000	7
iron	2,610	878	66
magnesium	35,900	22,700	37
manganese	470	193	59
sodium	324,000	250,000	23
Conventional Pollutants (mg/ℓ)			
BOD_5	1,700	360	79
TSS	1,500	260	83
oil and grease			
Nonconventional Pollutant (mg/ℓ)			
COD	3,900	800	79

* Priority pollutant.
** Flow-weighted average of two 24-hour composite samples.

grab sample of the primary sludge indicate that phenol may tend to concentrate in it.

Reductions of the metals found at levels significantly above their detection limits were good (50 to 70 percent), but was somewhat less than the reductions observed at Plants 12236 and 99999. As observed at Plants 12236 and 99999, little reduction was observed for calcium, magnesium, and sodium.

d. Discussion. The data obtained in the recent sampling effort indicate that VOC levels in pharmaceutical industry raw wastewater are significantly reduced through conventional biological treatment systems (i.e., air-activated sludge), and are reduced to a lesser degree in closed biological treatment systems (i.e., oxygen-activated sludge). Air stripping is believed to be a significant removal pathway because the data show that when there is a reduction in the possibility for air stripping, as occurs in the covered aeration basin of an O_2 system, a significant reduction in the removal of VOCs occurs.

It is important to note that EPA does not consider air stripping that occurs in sewer systems, equalization and other tanks, and biological treatment systems as treatment because the compounds are only transferred from one media to another. Consequently, VOCs are regarded as passing through POTWs if EPA does a pass-through analysis due to the potential for volatilization.

4. Biological Treatment System Costs

Information for estimating biological treatment system costs can be found in the technical record supporting final BCT effluent limitation guidelines or in the record supporting the March 9, ister Notice of Availability of Information.

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ontrol and treatment technologies, one of the erations is the ultimate disposal method used her a plant is a direct discharger to surface charger to POTWs, or a zero discharger can determining which technologies are most ing waste discharge. Table IV-9 summarizes harmaceutical manufacturing industry for process wastewater. This table was each plant's individual disposal methods osed Development Document).

the 464 manufacturing plants have hese plants also have minor indirect use zero discharge methods for some The majority of the industry are percent of the plants in EPA's

TABLE IV-9

SUMMARY OF WASTEWATER DISCHARGES

Methods of Discharge	Number of Plants in the Industry	Number of Plants by Subcategories			
		A	B	C	D
Direct Only	41	6	4	16	24
Direct with Minor Zero	7	2	4	5	4
Direct with Minor Indirect Discharge	4	1	1	2	3
Total Direct Dischargers	52	9	9	23	31
Indirect Only	264	24	54	77	216
Indirect with Minor Zero Discharge	20	4	7	10	13
Indirect with Minor Direct Discharge	1				1
Total Indirect Dischargers	285	28	61	87	230
SUBTOTAL	337	37	70	110	261
Zero Dischargers	127	0	9	26	109
TOTAL	464	37	79	136	370

Note: Subcategory counts will not equal industry totals because of multiple subcategory plants.

FATE OF WASTEWATER AT ZERO DISCHARGE PLANTS (TOTAL INDUSTRY)

Discharge Method	Zero Dischargers	Direct w/Zero	Indirect w/Zero
No Process Wastewater	96	1	0
Contract Disposal	7	2	6
Deep Well Injection	0	1	1
Evaporation	7	1	3
Land Application	5	2	
Ocean Dumping	1	0	
Recycle/Reuse	2	1	
Septic System	5	0	
Subsurface Discharge	2	0	
No Data	2	--	
TOTAL	127	7	

latest data base discharge to POTWs. One plant also has minor direct discharges, and another 20 use zero discharge techniques for some of their smaller wastestreams. Almost 27 percent of the manufacturing plants use only zero discharge methods (e.g., contract disposal, evaporation, ocean dumping, or complete recycling), or do not generate process wastewater requiring disposal. Seventy-six percent of the zero dischargers were classified as such because they generated no process wastewater requiring disposal.

1. Other Zero Wastewater Discharge or Disposal Methods

Other methods used to reduce or eliminate VOCs discharges include incineration, deep well injection, off-site treatment, and contract hauling. These methods all have potential application, but usually to a specific waste source, or under carefully studied and assessed conditions. a. Incineration. Gaseous or liquid solvents, flammable liquids, solids, tars, residues, or low-volume hazardous wastes can be incinerated. Combustion at high temperatures to break down toxic materials may be performed in properly designed incinerators, with or without auxiliary fuel, depending on the BTU value of the material being burned. However, additional scrubbing or particulate removal may be required on the gaseous products released from the incinerator (boiler).

b. Deep Well Injection. This approach has been used, but now carries critical legal connotations for protection of any adjacent aquifers contacted. Some states completely prohibit such disposal. EPA is developing guidelines on this under PL 93-523, covering potentially hazardous wastewater.

c. Off-site Treatment and/or Contract Hauling. Off-site treatment to a central treatment facility mutually owned or operated, either by pipeline or truck transport, may provide more economical treatment than an on-site facility. Pretreatment may be required depending on raw waste composition.

Contract hauling to another site may be applicable for small volume waste generators. However, this approach really only shifts the impact from one site to another.

Section X describes the procedures used to estimate compliance costs for individual plants. Costs were estimated for each plant with wastewater discharge. Section XI presents the economic impacts on individual plants.

VI. ECONOMIC CHARACTERISTICS AND OUTLOOK

One major source of pharmaceutical industry information is the data collected by the U.S. Bureau of the Census. The Census divides the pharmaceutical industry into three groups: Biological Products, such as blood derivatives and vaccines (SIC 2831); Medicinals and Botanicals, such as products extracted from animal organs and plant material (SIC 2833); and Pharmaceutical Preparations, mainly final products (SIC 2834).

A. INDUSTRY CHARACTERISTICS

From 1977 to 1982, the U.S. pharmaceutical industry as a whole grew in terms of both value of shipments and numbers of establishments and employees. However, not all SIC groups making up the industry grew during this period. The largest of the three pharmaceutical SIC groups is Pharmaceutical Preparations. During the 1977 to 1982 period, this SIC group declined in terms of numbers of companies, establishments and employees; the other two SIC groups grew in size during the same time period. Establishments in the pharmaceutical industry tend to be relatively specialized, with between 83 percent and 90 percent of the 1982 production at pharmaceutical plants being pharmaceutical products in a single SIC group. Likewise, most pharmaceuticals are produced by pharmaceutical establishments, as indicated by coverage ratios that range from 75 percent to 96 percent. Coverage ratios measure the percentage of pharmaceutical products that are produced by pharmaceutical plants. The rest is produced by plants that were not primarily pharmaceutical plants. Table VI-1 is a summary of the industry's characteristics. These data are discussed below.

1. Numbers of Companies, Establishments, and Employees

The Census of Manufactures is conducted by the U.S. Bureau of the Census on an establishment basis. Each establishment is classified in the particular industry (4 digit SIC group) that accounts for its major product (i.e. the value of that product exceeds in value its shipments of products in any other industry). A single company may own establishments in several industries. Therefore, the total number of companies in the pharmaceutical industry cannot be estimated by summing the number of companies in each of the relevant SIC groups. However, the data can be used to determine the relative size of each group and changes over time.

Pharmaceutical Preparations is the largest of the three SIC groups, with 579 companies owning establishments in the industry. The other two groups are about the same size: Biologicals had 277 companies in 1982 and Medicinals had 208 companies. During the 1977-82 period, the smallest SIC groups grew the fastest while the largest actually declined in terms of number of companies.

TABLE VI-1

PHARMACEUTICAL INDUSTRY CHARACTERISTICS

	SIC 2831 Biologicals		SIC 2833 Medicinals & Botanicals		SIC 2834 Pharmaceuticals Preparations	
	1977	1982	1977	1982	1977	1982
Number of Companies	249	277	154	208	655	579
Number of Establishments	310	367	177	227	756	686
Number of Employees (1,000)	15.7	23.1	14.4	17.7	126.4	125.0
Average Employment Size of Establishments	51	63	81	78	167	182
Value of Shipments ($ million)	899	2,254	1,890	3,391	11,459	19,062
Average Shipment per Plant ($ million)	2.9	6.1	10.7	14.9	15.2	27.8
New Capital Expenditures ($ million)	35	98	124	284	419	868
Specialization*	93%	90%	82%	83%	86%	89%
Coverage**	73%	78%	68%	75%	97%	96%

Source: 1977 and 1982 Census of Manufactures, U.S. Department of Commerce, Bureau of the Census.

* Specialization Ratio: The ratio of primary products (i.e., product in same SIC group as plant's SIC) shipments to total product shipments (primary and secondary) for the establishments.

** Coverage Ratio: The ratio of primary products shipped by establishments classified in the industry (SIC group) to the total shipments of such products that are shipped by all manufacturing establishments, wherever classified.

A similar picture results if SIC groups are described in terms of number of establishments. SIC 2834 is the largest group, with 686 establishments; this number declined from 756 between 1977 and 1982. The smallest group, SIC 2833, grew at the fastest rate from 177 establishments in 1977 to 227 establishments in 1982.

In terms of number of employees, SIC 2834 continues to be the largest. While employment fell slightly (about 1 percent) between 1977 and 1982, the decline was not as great as the decline in number of firms or establishments. As a result, the average number of employees per plant rose from 167 to 182, which is over twice as large as plants in the other two groups. The total number of employees grew in the other two SIC groups, and the average number per establishment increased in SIC 2831.

2. Value of Shipments

The order of these three SIC groups changes slightly if ranked in terms of value of shipments. The largest is SIC 2834, the second largest group is SIC 2833, and SIC 2831 is the smallest, even though shipments for SIC 2831 grew at the fastest rate in the 1977-82 period. The average shipments per establishment in 1982 ranged from $6.1 million in SIC 2831 to $27.8 million in SIC 2834.

3. New Capital Expenditures

The industry group with the fastest growing shipments in the 1977-82 period, SIC 2831, had the largest increase in new capital expenditures. The rate of increase in shipments for the other two groups was about the same and their rates of increase in new capital expenditures paralleled these rates. The high rate of capital expenditures in SIC 2831 is consistent with its large increase in number and size of establishments.

4. Specialization and Coverage

These three SIC groups tend to be highly specialized; i.e., plants concentrate on producing products in their own industry segment (SIC group). The establishments in SIC 2833 tend to be less specialized than those in the other two SIC groups. The coverage ratio measures the percent of the products in this industry made by plants in this industry, again measured on the basis of 4-digit SIC group. For Pharmaceutical Preparations, the coverage is extremely high; for the other two SIC groups, about 75 percent of the product is produced by plants in the industry.

B. OUTLOOK

Historically, the pharmaceutical industry has been characterized by its intensive research and development efforts, aggressive marketing, higher than average profit margins, multinational nature, and its high degree of involvement with regulatory agencies such as the Food and Drug Administration. These characteristics

remain basically unchanged in recent years. While the amount spent on R&D remains high, fewer companies are heavily involved in basic R&D work; and while their profit margins have returned to their previous high levels, 1985 saw a substantial drop in profit rates.

Pharmaceutical industry shipments are expected to continue to grow through 1991. However, two factors will slow the rate of increase in the value of shipments: 1) the market share for generic, and thus lower priced, prescription drugs is expected to increase, and 2) the market share for new drugs with higher unit values is expected to decrease. Pharmaceutical industry exports will benefit from the expected further decreases in the value of the dollar, which will make U.S. pharmaceuticals cheaper than otherwise for foreign buyers.

1. Value of Shipments

In the U.S. Census of Manufactures, value of shipments are presented for all the products produced by pharmaceutical establishments (Industry Data), and for all pharmaceuticals regardless of where produced (Product Data). As shown in Table VI-2, the data are very similar. Data are presented in terms of current dollars, and in constant 1982 dollars, which removes the influence of inflation.

Total industry shipments, measured in constant dollars, have continued to grow over the 1972 to 1986 period. However, the overall rate of growth has declined. For Biological Products, the value of shipments in constant dollars declined during the 1984-1986 period, with a rebound expected in 1987. The growth rate of Medicinals and Botanicals has steadily declined from 1972 to 1986, with a small rebound expected in 1987. The largest group, Pharmaceutical Preparations, was the slowest growing group and had a declining growth rate between 1972 and 1984. Since 1984, the growth rate has increased slightly over its rate of growth in the preceding five years.

The product data presents a similar picture except for Biological Products, which continued to grow during the 1984-86 period. The value of Medicinal and Botanical product shipments got between 1984 and 1986 in real terms while declining in current dollars because the prices of these goods fell during this period due to intense price pressure from foreign producers.

2. Trade Data

Both exports and imports of pharmaceuticals have been increasing over the 1972 to 1987 period. However, imports have been growing faster than exports, and the rate of increase for imports has been growing while the rate of increase for exports has been declining. The net result for pharmaceuticals overall is that exports are expected to barely exceed imports in 1987. Table VI-3 presents the trade data.

TABLE VI-2

VALUE OF SHIPMENTS - PHARMACEUTICAL INDUSTRY
(in Millions of dollars except as noted)

	1984	1985	1986	1987	Percent Change Compound Annual 1972-84	1979-84	1984-86
Industry Data							
Value of Shipments (current dollars)	28,967	31,443	33,426	--	11.3	10.9	7.4
2831 Biological Products	2,669	2,773	2,881	--	18.2	17.4	3.9
2833 Medicinal & Botanicals	3,410	3,435	3,410	--	17.2	7.7	0.0
2834 Pharm. Preparations	22,888	25,235	27,135	--	10.2	10.7	8.9
Value of Shipments (1982 dollars)	25,796	26,209	26,681	22,170	4.1	2.7	1.7
2831 Biological Products	2,626	2,549	2,591	2,635	11.8	12.9	-0.7
2833 Medicinal & Botanicals	3,613	3,758	3,870	3,990	10.4	5.5	3.5
2834 Pharm. Preparations	19,558	19,902	20,220	20,545	2.7	1.2	1.7
Product Data							
Value of Shipments (current dollars)	26,869	28,961	31,118	--	11.1	11.1	7.6
2831 Biological Products	2,779	2,995	3,245	--	15.5	14.4	8.1
2833 Medicinal & Botanicals	3,398	3,337	3,313	--	12.9	3.2	-1.3
2834 Pharm. Preparations	20,692	22,629	24,560	--	10.4	12.4	9.0

TABLE VI-2 (continued)

VALUE OF SHIPMENTS - PHARMACEUTICAL INDUSTRY
(in Millions of dollars except as noted)

					Percent Change Compound Annual		
	1984	1985	1986	1987	1972-84	1979-84	1984-86
Value of Shipment (1982 dollars)	23,861	24,377	24,970	25,560	3.9	2.9	2.3
2831 Biological Products	2,734	2,784	2,875	2,950	9.2	10.0	2.6
2833 Medicinal & Botanicals	3,630	3,683	3,795	3,910	6.4	1.2	2.3
2834 Pharm. Preparations	17,497	17,910	18,300	18,300	2.9	2.4	2.3

Source: U.S. Department of Commerce, 1987 U.S. Industrial Outlook. January 1987, p. 17-2.

TABLE VI-3

TRADE DATA - PHARMACEUTICAL INDUSTRY
(in millions of dollars except as noted)

	1984	1985	1986	1987	Percent Change Compound Annual 1972-84	1979-84	1984-86
Industry Data							
Value of Imports	1,665	1,896	2,359	3,020	17.3	15.5	21.9
2831 Biological Products	77	163	169	180	21.7	53.5	32.8
2833 Medicinal & Botanicals	1,341	1,517	2,028	2,700	16.1	12.5	26.2
2834 Pharm. Preparations	247	216	162	140	26.7	34.2	-17.2
Value of Exports	2,637	2,671	2,839	3,085	13.4	10.0	5.3
2831 Biological Products	456	516	603	700	18.7	9.1	15.3
2833 Medicinal & Botanicals	1,497	1,465	1,625	1,800	13.1	8.4	6.3
2834 Pharm. Preparations	684	691	611	585	11.7	15.1	-5.1
Net Trade Balance (Exports Minus Imports)	972	775	480	65			
2831 Biological Products	379	353	434	520			
2833 Medicinal & Botanicals	156	-52	-403	-900			
2834 Pharm. Preparations	437	475	449	445			

Source: U.S. Department of Commerce, 1987 U.S. Industrial Outlook, January 1987, p. 17-2.

The trade situation varies across the SIC groups. The fastest growth rates for both exports and imports have been experienced by Biological Products. The net result is a growing positive trade balance over the 1984 to 1987 period. The opposite case is true for Medicinals and Botanicals. Their growth rates have been slower, and the net trade balance has turned negative. This is particularly important for the overall picture since Medicinals and Botanicals comprise more than half of U.S. pharmaceutical exports and 80 percent to 90 percent of imports. In 1987, imports are expected to equal one and half times exports. While the trade balance for Pharmaceutical Preparations is expected to continue to be positive in 1987, the value of both exports and imports have declined during the 1984-87 period.

3. Profits

Up until 1985, profit rates for pharmaceutical companies remained very high and continued to exceed the profit rates of both chemicals and allied products and manufacturing in general. As shown in Table VI-4, in the 4th quarter of 1985, profit rates in both chemicals and allied products and in pharmaceuticals dropped precipitously, while manufacturing in general experienced a significant but much smaller drop in profits. However, based on data for the other quarters of 1985 and the first half of 1986, profit rates regained their traditionally high levels. The conclusion that profit rates have rebounded is further supported by examining second quarter 1987 earnings, which are higher than 1986 second quarter earnings for many large pharmaceutical companies. For example, out of a sample of 17 large drug firms, 14 had higher earnings in the 2nd quarter of 1987 than they had in the 2nd quarter of 1986. In addition, total 2nd quarter earnings for all 17 firms were 16 percent above total earnings in 2nd quarter 1986 (22).

The overall forecast is that the pharmaceutical industry will continue to be very profitable, in spite of growing competition from domestic producers of generic drugs and from foreign producers. The rate of growth of value of shipments (measured in terms of constant dollars) has slowed substantially in the past three years, as compared to the preceding decade or more. Likewise, the net balance of trade has declined to the point where the value of imports almost equals the value of exports. However, the profit levels for the industry have maintained their high levels, when compared to manufacturing in general. These continuing high profit rates are dependent on drug companies' ability to introduce new drugs that tend to be high priced and their ability to raise prices overall. In comparison to hospitalization, drugs are an economically efficient form of treatment and so are better able than health care in general to raise their prices.

TABLE VI-4

AFTER-TAX RATES OF PROFIT

Year (4th Quarter)	Profit per Dollar of Sales (Cents)			Profit on Stockholders' Equity (Percent)		
	Pharmaceuticals	Chemicals and Allied Products	All Manufacturing	Pharmaceuticals	Chemicals and Allied Products	All Manufacturing
1972	10.1	6.3	4.4	18.3	12.8	11.5
1973	10.7	6.9	4.6	17.7	14.4	13.4
1974	12.2	8.3	5.7	15.9	14.8	13.2
1975	10.7	7.6	5.1	15.6	15.2	13.1
1976	12.6	7.5	5.3	16.5	12.8	13.1
1977	11.7	6.7	5.3	17.4	13.8	14.4
1978	11.3	7.7	5.6	17.0	16.3	16.1
1979	11.9	7.0	5.3	17.9	15.3	15.7
1980	11.3	6.3	4.8	16.9	13.3	14.1
1981	12.4	6.7	4.3	18.6	13.3	12.0
1982	14.6	4.8	2.8	21.3	8.8	7.2
1983	14.1	5.2	4.4	21.8	11.1	12.0
1984	12.6	5.2	4.1	19.3	10.4	11.0
1985	2.8	1.5	3.4	4.3	3.1	9.3
1986 (2nd Quarter)	12.9	7.0	4.7	19.6	14.9	12.2

Source: U.S. Federal Trade Commission, Quarterly Financial Report for Manufacturing Mining, and Trade Corporations, various issues.

VII. PRODUCT GROUPS - DESCRIPTION AND OUTLOOK

The value of pharmaceutical final products grew faster in the 1977-82 period than they did in the 1972-77 period (measured in current dollars). An exact comparison cannot be made due to a creation of a new category of products (diagnostic substances) by the Bureau of the Census. However, the compound annual rate of growth in the earlier period was approximately 9.4 percent as opposed to 12.4 percent in the later period. During the 1977-82 period, three groups of products grew much faster than the overall industry: products affecting the cardiovascular system, products affecting parasitic and infectious diseases, and products for veterinary use. At the same time, preparations for the skin, and blood and blood derivatives grew at a much lower rate than pharmaceuticals in general. Detailed descriptions of the major product groups follow. All are final products and all but two of these product groups are part of SIC 2834. The last two groups on the list (blood and blood derivatives for human use, and active and passive immunization agents) are part of SIC 2831. The remaining pharmaceuticals products included in SIC 2831 and SIC 2833 are intermediate products used as inputs for final products. Table VII-1 presents information on the value of shipments for each product group discussed.

A. PREPARATIONS AFFECTING NEOPLASMS, ENDOCRINE SYSTEM AND METABOLIC DISEASES

This group includes a fairly diverse collection of pharmaceutical products. Shipments of $1,724 million were recorded in 1982, accounting for 9.9 percent of the final products shown in Table VII-1. Value of shipments for this group increased 13.9 percent percent annually, while pharmaceutical shipments overall grew 12.4 percent annually. In addition, this was substantially higher than its 7.9 percent growth rate in the 1972-77 period.

Hormones accounted for nearly 85 percent of total group shipments. Secreted by the endocrine glands (thyroid, pituitary, gonads, and others) and present only in minute quantities, natural hormones regulate the body's metabolic activities. Hydrocortisone, androgens, estrogens, and progestogens are examples of steroid hormones. Corticotropin and insulin are nonsteroidal hormones. Hormone shipments increased at a rate of about 15 percent a year between 1977 and 1982. Ten out of the 200 most prescribed drugs in 1980 were oral contraceptives. Topical and systemic corticoids (used as anti-flammatory agents) account for 17 percent of group shipments and show an average annual increase of 9.6 percent from 1977 to 1982. Insulin and antidiabetic agents had shipment increases above the industry average.

To summarize, this product group has exhibited a higher than average rate of increase in shipments in years 1977-82. In contrast during the preceding five years its growth rate was lower than the industry average.

TABLE VII-1

PHARMACEUTICAL FINAL PRODUCTS - VALUE OF SHIPMENTS
BY ALL PRODUCERS (current dollars)

Product Class	Value of Shipments (Million of Dollars) 1972	1977	1982	Compound Annual Rate of Change (Percent) 1972-77	1977-82
Preparations affecting neoplasms, endocrine system and metabolic disease	615	900	1,724	7.9	13.9
Preparations affecting central nervous system and sense organs	1,636	2,231	4,003	6.4	12.4
Preparations affecting cardiovascular system	400	751	1,938	13.4	20.9
Preparations affecting respiratory system	561	896	1,580	9.8	12.0
Preparations affecting digestive and genito-urinary systems	746	1,074	1,410	7.6	13.6
Preparations affecting the skin	344	621	825	12.5	5.9
Vitamins, nutrients and hematinics	587	1,302	2,093	17.3	10.0
Preparations affecting parasitic and infectious diseases	948	1,285	2,592	6.3	15.1
Preparations for veterinary use	214	354	811	10.6	18.0
Blood and Blood derivatives for human use	126	243	361	14.0	8.2

TABLE VII-1 (continued)

PHARMACEUTICAL FINAL PRODUCTS - VALUE OF SHIPMENTS
BY ALL PRODUCERS (current dollars)

Product Class	Value of Shipments (Million of Dollars) 1972	1977	1982	Compound Annual Rate of Change (Percent) 1972-77	1977-82
Active and passive immunization agents and therapeutic counterparts	89	126	*	7.2	*
Total, incl. last group	6,266	9,783	*	9.3	*
Total, excl. last group	6,177	9,657	17,337	9.4	12.4

* Change of definition in 1982 makes comparison not possible.

Source: U.S. Census of Manufactures, various years.

B. PREPARATIONS AFFECTING CENTRAL NERVOUS SYSTEM AND SENSE ORGANS

The largest of all groups, the value of shipments for this group accounted for 23 percent of shipments for all product groups. Shipments increased 12.4 percent annually from 1977 to reach $4,003 million in 1982. Important subgroups are internal narcotic and nonnarcotic analgesics and antipyretics, psychotherapeutic agents, Central Nervous System (CNS) stimulants, sedatives and hypnotics, anesthetics, and eye and ear preparations.

Analgesics reduce awareness of pain without loss of consciousness; antipyretics help lower body temperature. The narcotic analgesics include morphine and its derivatives, synthetic morphine-like drugs and synthetic moieties of morphine molecules. While shipments of narcotic analgesics were nearly unchanged between 1977 and 1982, nonnarcotic analgesics (including aspirin, phenacetin, and acetaminophen) had 1982 shipments of $1,744 million with an average annual increase since 1977 of 18.5 percent. Aspirin, aspirin combinations and other salicylates yielded $558 million in shipments. While the narcotic analgesics require prescriptions (referred to as ethical drugs), most of the nonnarcotic analgesics do not (referred to as proprietary drugs). Also included in this group are the nonhormonal antiarthritics.

Amphetamines, a major subgroup of CNS stimulants, typically are used to reduce fatigue or appetite (anti-obesity drugs). Amphetamine shipments decreased during the 1977-82 period. Stimulants as a whole had constant shipments over this period.

Sedatives and hypnotics (sleep inducing agents) shipments fell during the 1982-87 period. This was due in part to the introduction of a number of new nonbarbiturate drugs in the late 1970s.

General and local anesthetic shipments grew 12.8 percent annually from 1977 to reach $161 million in 1987. Most of the growth in this subgroup has been in general anesthetics.

In summary, the largest product group in terms of value of shipments has experienced a growth rate equal to that for all pharmaceutical products in years 1977-82. This is in contrast to the preceding five years when this product group had the lowest growth rate (6.4 percent annually).

C. PREPARATIONS AFFECTING THE CARDIOVASCULAR SYSTEM

This group of products had the highest increase in rate of shipments of all eleven groups, with an annual rate of increase of 20.9 percent. Total 1982 shipments were $1,938 million, while 1977 shipments were $751 million. This drug market appears promising because a number of new drugs with far-ranging possibilities, notably calcium and beta blockers, have entered the market in recent years.

Anticoagulants are agents that delay or counteract blood coagulation and are used to reduce or prevent blood clot formation within blood vessels. Shipments in 1982 were valued at $103 million, having grown 24.2 percent annually since 1977. Hypotensives help control hypertension and its effects, particularly high blood pressure. The major hypotensives contain rauwolfia compounds derived from an herb. Data for total 1982 shipments of hypotensives is not available.

Vasodilators induce smooth and cardiac muscle relaxation and dilate the blood vessels. Shipments in 1982 were estimated at $339 million, having increased 16.8 percent annually since 1977. The last major subgroup includes vasopressors, antiarrhythmics and antiheparin agents. Vasopressors constrict blood vessels and thus raise blood pressure. Antiarrhythmics help the irregular, rapid heartbeats known as arrhythmias (a potentially fatal condition for those with weak or diseased hearts). The beta and calcium blockers are perhaps the most important new drugs in this group. Calcium blockers prevent calcium and minerals from entering muscle tissues and thus ease the pain of angina. Calcium blockers have fewer side effects than beta blockers, which try to influence the hormonal system that can speed up the heart and other organs' action in times of stress. Shipments in 1982 for this subgroup were $801 million, with a growth rate of 31.9 percent annually, from 1977 to 1982.

In summary, this product group has been experiencing very rapid growth in shipments. It was the second fastest growing product group in the 1972-77 period and the fastest growing group in the 1977-82 period.

D. PREPARATIONS AFFECTING THE RESPIRATORY SYSTEM

This product group's shipments increased 12.0 percent annually from 1977 to 1982, slightly below the overall pharmaceutical industry average of 12.4 percent. With 1982 shipments of $1,580 million, this group accounted for 9.1 percent of all pharmaceuticals. Cold preparations, both ethical and proprietary, nose drops, lozenges, nasal decongestants and antihistamines are included in this product group. Cold preparations include combinations of antibiotics, nasal decongestants, antihistamines, analgesics, and bioflavanoids. Bronchial dilators, agents that open the lungs, bronchi, and bronchial tubes making breathing easier, and cough preparations, both narcotic (those with codeine) and nonnarcotic, had shipment increases greater than the pharmaceutical industry average. Antihistamines are complex amines that prevent the buildup of histamines in body tissues and are typically used for treatment of allergenic diseases. They are also used in nasal and ophthalmic decongestants, sleep inducers, and antipruritics (for relief of itching).

E. PREPARATIONS AFFECTING THE DIGESTIVE AND GENITO-URINARY SYSTEMS

This product group accounted for $1,410 million dollars in value of shipments in 1982 and represented 8 percent of total pharmaceutical product shipments. Antacids, the largest subgroup in this category, with $417 million in 1982 shipments, have experienced a growth rate of 6.8 percent annually since 1977. Antacids reduce excess gastric acidity by several methods: neutralization; buffering; a combination of absorption, buffering and partial neutralization; or ion-exchange. Sodium bicarbonate, sodium citrate, sodium acetate, magnesium oxide, calcium carbonate, and aluminum hydroxide gel are common active ingredients in antacids. Antacids are mainly proprietary drugs. For both antacids and laxatives there is intense competition and the rising costs for advertising will become an important factor in sales growth in the near future. Phenolphthalein, castor oil, dioctyl sodium, and calcium sulfosuccinates are all active ingredients in laxatives. Antispasmodics and anticholinergenics are drugs that relax involuntary (smooth) muscles and help relieve discomfort from peptic ulcers and asthma.

Diuretics, agents that promote urine excretion, have been an important growth market. Data for 1982 are not available due to confidentiality. While diuretics increase urine, sodium, and chloride excretion, many also promote potassium excretion. Perhaps the biggest area for sales growth is with "potassium sparing" diuretics. A number already exist, with others slated for release.

F. PREPARATIONS AFFECTING THE SKIN

The value of shipments for this group increased only 5.9 percent annually between 1977 and 1982. Dermatological preparations, used for treatment of skin disorders, represented 60 percent of group shipments and increased only 4.7 percent annually. Other drugs contained in this group are hemorrhoidal preparations and external analgesics.

G. VITAMINS, NUTRIENTS AND HEMATINIC PREPARATIONS

This group had 1982 shipments of $2,093 million and accounted for 12 percent of total pharmaceutical product shipments. This group's shipments have been increasing strongly since the 1960s; the average annual growth in shipments from 1977 to 1982 was 10.0 percent and from 1967 to 1977 was 13.4 percent.

Vitamins are necessary in small quantities for normal metabolism and are most often marketed as dietary supplements. They are also used medicinally to prevent or treat disease. Most of vitamin production is by chemical synthesis. Bulk vitamins are formulated either as pills or capsules and are frequently used by the animal feed and food additive industries. From 1977 to 1982, multivitamin shipments increased annually at 13.9 percent.

H. PREPARATIONS AFFECTING PARASITIC AND INFECTIOUS DISEASES

Included in this group are amebicides, anthelmintics, antibiotics, tuberculostatic agents, antimalarials, sulfonamides, antifungal preparations, antibacterials, and antiseptics. In terms of total 1982, shipments, this was the second largest group, with $2,592 million. The growth rate for value of shipments slowed to 6.3 percent annually from 1972 through 1977, but jumped to 15.1 percent in the 1977-82 period. Over 70 percent of total shipment value was due to shipments of antibiotics in 1977. Comparable figures are not available for 1982.

Broad and medium spectrum antibiotics (not including penicillin) grew at an annual rate of 15.1 percent; this subgroup includes tetracycline and its derivatives, erythrocin, cephalosporins and chloramphenicol. Cephalosporins have seen a number of new developments in recent years. They are substances chemically related to penicillins but have a broader spectrum of activity and lower acute toxicities than penicillins. Penicillin shipments grew at a slower rate of 7.1 percent annually. Most likely, shipments will continue to grow at a slow rate as more and more pathogens become resistant to penicillin. However, a number of popular antibiotics are semi-synthetic penicillins; the precursor to penicillin is produced by fermentation and then chemically altered to increase effectiveness.

Sulfonamides, or sulfa drugs, have been gradually replaced by antibiotics in treating bacterial infections, but shipments growth rate (18.2 percent annually) is above the group average. They are used in diuretics, hypoglycemics, and hemotherapeutics. Antibacterials and antiseptics have shown slow growth from 1977 to 1982 (6.0 percent annually) but represent only 8 percent of value of shipments for the group in 1977.

I. PREPARATIONS FOR VETERINARY USE

This group includes all health, vitamin and nutrient products formulated for veterinary use. There were over $811 million worth of shipments in 1982 representing 4.7 percent of total shipments for all product groups. Average annual growth from 1977 to 1982 (18.0 percent) was much higher than for pharmaceuticals overall.

J. BLOOD AND BLOOD DERIVATIVES FOR HUMAN USE

Included in this group are whole human blood, blood plasma, normal blood serum, and other blood fractions. Total shipments in 1982 were $361 million, or only 2 percent of all pharmaceuticals. The growth rate for this group, at 8.2 percent,
was below the industry average.

K. PREPARATIONS FOR ACTIVE AND PASSIVE IMMUNIZATION AND THERAPEUTIC COUNTERPARTS

Comparable product value data are not available for 1982 due to

changes in Census Bureau definitions. However, total 1977 shipments for this group were only $126 million, having shown a average annual increase of 7.2 percent since 1972. A slow growth rate in the subsequent period is expected. Toxoids, antigens, and viral vaccines are used in active immunization. An active immunization agent alerts the body's immunological defense system and causes it to form antigens and antibodies to deal with a possible future pathogen. Passive immunization agents, like antitoxins, help the body deal with a pathogen that has breached the body's defenses. Antivenins, antitoxins, immune globulins, and immune serums are agents of passive immunization.

VIII. FINANCIAL ANALYSIS OF PHARMACEUTICAL FIRMS

The following section describes the financial condition of the pharmaceutical industry based on recent data from publicly-held pharmaceutical companies. This analysis focuses on publicly-held companies for several reasons. First, the data are readily available and are appropriate for the level of detail needed for this preliminary analysis. Second, these companies provide a reliable preliminary assessment of the industry. Publicly-held pharmaceutical companies form the majority of the industry in terms of both total sales and number of establishments. Based on the industry data previously collected by EPA (under authority of Section 308 of the Clean Water Act), 93 publicly-held companies owned 279 establishments, while the 152 private firms owned only 185 pharmaceutical establishments.

For this analysis, six years of financial data from 43 publicly-held companies were obtained from Standard and Poors COMPUSTAT Services. In most cases, this data covered the years 1981-1986. In a few cases, the data were for an earlier period, such as 1979-84.

A. RATIO ANALYSIS

Financial ratios are frequently used to identify companies with operating and/or financial difficulties. Since the ratios are calculated using data available from balance sheets and income statements, they are widely applicable. This makes it relatively easy to compare industries and to compare companies within an industry.

Four types of ratios are presented, which measure profitability, liquidity, solvency, and leverage. For most ratios, there are "rules of thumb" which can be used to determine whether the company is financially healthy. In addition, pharmaceutical industry ratios are available from Robert Morris Associates (RMA), based on information collected from commercial loan applications. These ratios were used for comparison purposes: RMA ratios were used to judge whether the sample used is representative, and the rules of thumb were used to determine if the companies are better off financially than manufacturing companies in general.

B. PROFITABILITY

The first financial question usually asked concerns the profitability of the operation. In this analysis, profitability is measured in two ways, return on total assets and return on sales. The return on total assets measures how effectively the operation is being managed. Since RMA measures this in terms of profit before taxes, the before tax measure is used here. Based on 94 drug company loan applications during 1985-1986, as reported by RMA, median profits before taxes were 8.4 percent of total assets. For these same companies, the upper quartile profit rate was 19.3

percent and the lower quartile rate was 1.7 percent of total assets. For the 43 companies in our sample and shown in Table VIII-1, average profitability over six years ranged from a high of 53.0 percent (Mylan Laboratories) to a low of -1.70 percent (A. H. Robins). The median profitability for the 43 companies is 11.6 percent. In general, these companies have been somewhat more profitable than those included in the RMA sample. There appears to be no relationship between size of company (as measured in terms of total assets) and the profitability of the company. Both the most profitable and the least profitable are among the smallest companies.

The second measure of profitability is return on sales, i.e., profits as a percentage of sales. Based on loan applications in 1985-86 from 94 drug companies, as reported by RMA, median profits before taxes were 6.1 percent of sales. For the 43 publicly held companies in the sample and shown in Table VIII-1, the average profitability over six years ranged from a high of 37.4 percent (Mylan Laboratories) to a low of -4.03 percent (Sceptre Resources Inc.). The median profitability for the 43 companies is 11.83 percent. As with return on assets, these companies are somewhat more profitable than those in the RMA sample. Again, there is no relationship between size and profitability.

C. LIQUIDITY

Liquidity ratios measure the firm's ability to meet its maturing short-term obligations. This is particularly relevant to a financial officer when evaluating whether or not a company should borrow more money. The most commonly used measure of short-term solvency is the current ratio. This ratio is computed by dividing current assets by current liabilities, and it indicates the extent to which the claims of short-term creditors are covered by assets that can be converted to cash in a roughly corresponding period. The rule of thumb for a healthy liquidity position is a current ratio of 2.0, i.e., current assets, including inventory, are twice current liabilities. This allows the company to cover its current liabilities without liquidating all current assets. Based on RMA data, the current ratio for pharmaceutical companies had a median value of 1.9, with an upper quartile of 3.5 and a lower quartile of 1.4. The average current ratio for our 43 publicly-held companies ranged from a high of 6.2 (Bolar Pharmaceutical Co.) to a low of 1.7 (Abbott Laboratories). The median current ratio is 2.32. Pharmaceutical companies generally are in a strong position visa-vis liquidity, and the publicly-held companies are in a particularly strong position.

A second liquidity ratio commonly used is the quick ratio, or acid test. This is a more conservative measure in that it does not include inventories in current assets. Since inventories are usually the least liquid of a firm's current assets, they are most likely to be sold at a loss in the event of liquidation. The

TABLE VIII-1

FINANCIAL RATIOS OF 43 PUBLICLY OWNED PHARMACEUTICAL FIRMS

	Company Name	Total Assets (Million $)	Net Sales (Million $)	Profits Before Taxes as Percent of Total Assets	Profits Before Taxes as Percent of Sales	Financial Ratios: Current Ratio	Quick Ratio	Beaver's Ratio	Leverage Ratio
1	Abbott Laboratories	3,042.25	3,024.12	19.72	19.84	1.65	0.92	0.40	1.00
2	Alza Corp.	71.24	29.82	9.25	22.10	3.96	3.24	0.35	4.71
3	American Cyanamid	3,252.87	3,641.16	7.44	6.64	1.92	1.29	0.25	1.04
4	American Home Products	3,184.87	4,611.08	35.54	24.55	3.12	2.10	1.02	0.61
5	American Hospital Supply	1,877.21	2,829.03	12.45	8.26	2.32	1.21	0.33	0.71
6	Astra Corp.	1.47	2.52	7.55	4.40	1.49	0.50	0.23	1.23
7	Baxter Travenol Lab	3,569.71	2,452.72	5.34	7.78	1.86	1.00	0.24	2.62
8	Becton, Dickinson & Co.	1,210.27	1,146.96	8.92	9.41	2.31	1.36	0.26	0.96
9	Bio-Rad Laboratories	65.05	80.49	5.69	4.60	2.28	1.14	0.11	1.90
10	Block Drug	240.23	247.87	12.70	12.31	2.55	1.29	0.44	0.46
11	Bolar Pharmaceutical Co.	33.11	30.38	30.41	33.15	6.22	3.68	1.92	0.13
12	Bristol-Myers Co.	3,234.13	4,080.47	22.80	18.07	2.48	1.65	0.51	0.58
13	Carter-Wallace, Inc.	280.66	345.68	12.44	10.10	2.34	1.45	0.32	0.72
14	Chattem, Inc.	48.76	58.69	9.50	7.89	2.12	1.25	0.22	0.73
15	Cooper Companies, Inc.	410.75	275.98	3.29	4.89	2.34	1.53	0.21	0.90
16	Del Laboratories, Inc.	61.12	83.40	9.23	6.76	2.38	1.21	0.16	1.88
17	Dexter Corp.	424.34	585.88	11.61	8.41	2.16	1.21	0.23	1.48
18	Forest Laboratories, Inc.	55.03	30.63	11.12	19.98	4.70	3.51	0.67	0.46
19	ICN Pharmaceuticals, Inc.	167.37	55.81	0.88	2.65	3.18	2.21	0.12	1.41
20	Johnson & Johnson	4,667.43	6,113.56	15.50	11.83	2.44	1.39	0.47	0.79
21	Key Pharmaceuticals, Inc.	97.57	96.33	17.52	17.74	2.70	1.38	0.42	1.19
22	Lee Pharmaceuticals	9.59	17.86	17.52	9.40	2.49	1.41	0.33	0.79
23	Lilly (Eli) & Co.	3,610.76	3,144.97	20.90	24.00	1.94	1.12	0.48	0.68
24	Marion Laboratories	181.07	228.99	22.75	17.99	2.37	1.58	0.59	0.51
25	Merck & Co.	4,295.04	3,412.44	17.90	22.53	1.97	1.33	0.50	0.80
26	Monsanto Co.	7,015.36	6,648.11	6.67	7.04	2.00	1.17	0.36	1.72
27	Mylan Laboratories	38.91	55.02	52.96	37.46	5.54	3.23	1.50	0.53
28	North American Biological	8.41	26.92	0.56	0.17	1.91	0.96	0.32	1.32
29	Pfizer, Inc.	4,167.59	3,801.38	17.34	19.01	2.05	1.19	0.32	1.04
30	Reid Rowell	11.28	10.87	9.04	9.38	3.23	2.11	0.36	0.76

TABLE VIII-1 (continued)

FINANCIAL RATIOS OF 43 PUBLICLY OWNED PHARMACEUTICAL FIRMS

	Company Name	Total Assets (Million $)	Net Sales (Million $)	Profits Before Taxes as Percent of Total Assets	Profits Before Taxes as Percent of Sales	Financial Ratios: Current Ratio	Quick Ratio	Beaver's Ratio	Leverage Ratio
31	Revlon Group, Inc.	951.36	973.25	2.10	2.05	2.13	1.19	0.15	1.02
32	Robins (A.H.) Co.	597.84	604.10	-1.70	-1.68	3.05	2.14	0.10	-4.74
33	Rorer Group	515.50	490.79	12.10	12.70	2.05	1.27	0.27	-1.81
34	Sceptre Resources Ltd.	153.29	19.98	-0.53	-4.03	2.06	2.06	0.11	3.19
35	Scherer (R.P.)	185.01	182.23	8.29	8.41	2.12	1.34	0.14	0.57
36	Schering-Plough	2,567.28	1,939.22	10.60	14.03	1.67	1.06	0.21	0.86
27	Smithkline Beckman Corp.	3,176.66	2,956.77	21.56	23.16	1.88	1.31	0.49	1.29
38	Squibb Corp.	2,136.96	1,777.66	12.12	14.57	2.15	1.34	0.36	0.80
39	Sterling Drug, Inc.	1,478.14	1,843.62	17.85	14.31	2.47	1.63	0.35	0.70
40	Syntex Corp.	1,085.05	873.24	16.09	20.00	2.23	1.56	0.45	0.69
41	Upjohn Co.	2,239.95	2,038.12	11.46	12.59	2.05	1.15	0.29	0.91
42	Warner-Lambert Co.	2,769.51	3,200.65	8.44	7.30	1.78	1.01	0.18	1.63
43	Zenith Laboratories, Inc.	35.23	42.59	16.61	13.73	2.93	1.59	0.49	0.77

Source: Meta Systems, Inc. calculations based on financial data obtained from Compustat Services, Inc.

common rule of thumb for a healthy financial position is a quick ratio of 1.0; i.e., cover all current liabilities with current assets not including inventories. Based on RMA data, quick ratios for pharmaceutical firms are generally strong. The median ratio is 1.1, with an upper quartile of 2.1 and a lower quartile of 0.6.

The quick ratios for our 43 publicly-held companies also tend to be strong. The average ratios range from a high of 3.68 (Bolar Pharmaceutical Co.) to a low of 0.50 (Astra Corp.) with a median quick ratio of 1.34.

Taken together, the two liquidity ratios indicate that only one of these 43 companies has potential liquidity problems and two other companies are borderline. There are 10 companies with current ratios below 2.0. However, seven of these have quick ratios greater than 1.0 and thus are not interpreted to have liquidity problems. One company (Astra Corp.) clearly has a potential problem, with a current ratio of 1.49 and a quick ratio of 0.50. It is the smallest company in the sample and has a profitability rate below the median. The next smallest company (North American Biological) is borderline in terms of liquidity (current ratio of 1.91 and quick ratio of 0.96). This company has a more significant problem in terms of its very small average profits. The other company with borderline liquidity problems (Abbott Laboratories with a current ratio of 1.65 and a quick ratio of 0.92) has very high profits.

D. SOLVENCY

Beaver's Ratio is designed to assess the short-term solvency of a firm. It has been found to be a good predictor of business bankruptcy, although recent literature has been critical of this test. The ratio compares internally generated cash flow (net income after taxes plus depreciation) to total debt (current liabilities plus long-term debt). Generally, if the ratio is greater than 0.2, the firm is judged to be solvent. If the ratio is less than 0.15, the firm is judged to be insolvent. Ratios between 0.15 and 0.2 indicate that solvency/insolvency is uncertain. RMA does not calculate Beaver's Ratio.

Beaver's Ratio was calculated for each of the 43 publicly-held companies in our sample. The values ranged from a high of 1.92 (Bolar Pharmaceutical Co.) to a low of 0.10 (A. H. Robins Co.). The median value is a healthy 0.35. Further indication of the general health of this industry is that only five of the 43 companies have a Beaver's Ratio of less than 0.15, and three have a ratio between 0.15 and 0.20.

E. LEVERAGE

Leverage ratios compare the amount of funds supplied by the owners of the company to the amount of funds provided by the firm's

creditors. For several reasons, creditors are less willing to loan money when the debt equity ratio is high. First, if the owners provide only a small proportion of total financing, then the risks of the enterprise are borne mainly by the creditors. Likewise, if the firm earns more on the borrowed funds than it pays in interest, the return to the owner is magnified. However if it earns less, then the differential must be made up from the owner's share of the profits. In times of economic downturns, firms with low leverage ratios have less risk of loss. There are no rules of thumb for debt-equity ratios, since the amount of leverage desirable is a function of the industry's operating characteristics. Based on RMA data, the median debt-net worth ratio for pharmaceutical firms was 1.2, with an upper quartile of 0.4 and a lower quartile of 3.1.

The average debt equity ratio for the 43 publicly-held firms ranged from 0.13 (Bolar Pharmaceutical Co.) to 4.71 (Alza Corp.), with a median value of 0.90. Therefore, these 43 firms have relatively less debt than the sample covered by RMA. Two firms had negative debt-equity ratios. (A. H. Robins and Rorer Group). In the case of A. H. Robins, this negative value is the result of negative equity in two years and of intangibles having a value greater than equity in three years. In the case of Rorer Group, this negative value is due to one year when equity was negative combined with several years when the debt equity ratio was very small.

F. SUMMARY

In general, the financial condition of pharmaceutical companies is strong. In a few cases, companies have problems as indicated by one or more of the ratios. However, none of the companies fail all the ratios. Companies with very high debt equity ratios and low leverage ratios may have problems raising significant amounts of capital through borrowing. For large companies, this might result in their paying higher interest rates. For small companies, this might result in their not being able to raise the funds at all, even at higher interest rates.

SECTION IX. PHARMACEUTICAL PLANT PROFILE

The location and size (both in terms of employment and sales) of 464 pharmaceutical plants that might be covered by regulation are described below. This discussion supplements Section II of the Development Document, which presents information on 465 plants. Since that document was written, one plant has been removed due to uncertainty about its status. Therefore, this report presents information on, and analyzes, 464 plants.

A. GEOGRAPHICAL DISTRIBUTION OF THE INDUSTRY

Table IX-1 shows the geographical distribution of plants in terms of number of plants, their sales, and their employment. These data were originally compiled for earlier analyses of the pharmaceutical industry. A comprehensive list of 464 pharmaceutical plants was identified and data were gathered via Section 308 surveys conducted in 1978 and 1979. The employment data in Table IX-1 are from those surveys. The sales data represent plant-level sales in 1979, as estimated by Economic Information Systems, Inc. and Meta Systems, Inc.

In terms of number of plants, the pharmaceutical industry is concentrated in EPA Region II (with 36 percent of the plants), followed by Regions V (with 19 percent), IV (with 11 percent), III (with 9 percent) and IX (with 9 percent). The states and territories containing the largest number of plants are: New Jersey (with 16 percent of the plants), Puerto Rico (with 10 percent), New York (with 9 percent), and Illinois and California (with 8 percent each). While all EPA regions have some plants, 12 states do not have any pharmaceutical plants.

The distribution of pharmaceutical sales across regions is similar to the distribution in terms of number of plants. However, the plants in Region V tend to be much larger on average, and so Region V accounts for over one-third of pharmaceutical sales. Region II is sightly smaller with 33.5 percent of sales. Trailing these two are Regions IV (with 9 percent) and IX (with 7 percent). The states with the largest pharmaceutical sales are: New Jersey (with 21 percent of the sales), Indiana (with 13 percent), Illinois (with 12 percent) and Puerto Rico (with 11 percent).

Regions II and V are also the most important in terms of number of employees. Region II accounts for 39 percent and Region V for 32 percent of pharmaceutical employment. The next largest is Region IV with only 12 percent of the employment, followed by Regions IX (6 percent) and VI (5 percent). The states with the greatest pharmaceutical employment are: New Jersey (with 21 percent of the employment), Indiana (with 12 percent), Illinois (with 11 percent), and New York and Puerto Rico (with 9 percent each).

TABLE IX-1

PHARMACEUTICAL PLANT PROFILE BY PLANT,
SALES BY PLANT, SALES, EMPLOYMENT

Location	Number of Plants	% of Total	Sales ($000)	% of Total	Employ	% of Total
REGION I						
CT	7	1.51	138,198	0.83	324	0.32
ME						
MA	7	1.51	120,493	0.72	584	0.58
NH						
RI	1	0.22	22,613	0.14	73	0.07
VT	1	0.22	11,663	0.07	33	0.03
Total	16	3.45	292,967	1.76	1014	1.00
REGION II						
NJ	75	16.16	3,570,921	21.43	21,313	21.00
NY	43	9.27	150,422	8.90	9,065	8.93
PR	46	9.91	1,861,798	11.17	8,797	8.67
VI	2	0.43				
Total	166	35.77	5,583,141	33.50	39,175	38.60
REGION III						
DE	2	0.43	18,600	0.11	241	0.24
MD	6	1.29	67,281	0.40	402	0.40
PA	27	5.82	304,218	1.88	897	0.88
VA	7	1.51	304,218	1.83	897	0.88
WV	2	0.43	57,002	0.34	299	0.29
DC						
Total	44	9.48	751,319	4.51	2,736	2.69
REGION IV						
AL	3	0.65	6,024	0.04	44	0.04
GA	6	1.29	182,832	1.10	1,132	1.12
FL	8	1.72	135,782	0.81	752	0.74
MS	2	0.43	197,000	1.18	1,517	1.49
NC	12	2.59	502,520	3.02	5,476	5.40
SC	3	0.65	72,682	0.44	261	0.26
TN	10	2.16	419,179	2.52	2,947	2.90
KY	5	1.08	31,781	0.19	59	0.06
Total	49	10.57	1,547,800	9.3	12,188	12.01
REGION V						
IL	38	8.19	2,079,952	12.48	11,612	11.44
IN	17	3.66	2,187,365	13.12	11,704	11.53
OH	14	3.02	553,433	3.32	2,842	2.80
MI	14	3.02	1,088,433	6.53	5,617	5.58
WI	4	0.86	54,874	0.33	215	0.21
MN	4	0.86	25,058	0.15	163	0.16
Total	91	19.16	5,989,115	35.98	32,153	31.67

TABLE IX-1 (continued)

PHARMACEUTICAL PLANT PROFILE BY PLANT,
SALES BY PLANT, SALES, EMPLOYMENT

Location	Number of Plants	% of Total	Sales ($000)	% of Total	Employ	% of Total
REGION VI						
AR	2	0.43	225,500	1.35	3,116	3.07
LA	2	0.43	9,800	0.06	18	0.02
OK						
TX	13	2.80	266,008	1.60	1,523	1.50
NM						
Total	17	3.66	501,308	3.01	4,657	4.59
REGION VII						
IA	3	0.65	71,800	0.43	231	0.23
KS	4	0.86	123,186	0.74	494	0.49
MO	18	3.38	483,658	2.90	2,064	2.08
NE	4	0.86	87,300	0.52	803	0.79
Total	29	6.25	765,944	4.59	3,592	8.54
REGION VIII						
CO	5	1.08	69,233	0.42	362	0.36
UT	1	0.22	70,200	0.42	17	0.02
WY						
MT						
ND						
SD						
Total	6	1.3	139,433	0.84	379	0.38
REGION IX						
AZ	1	0.22	13,900	0.08	6	0.01
CA	38	8.19	1,056,268	6.34	5,469	5.39
NV	1	0.22	24,632	0.15	115	0.11
HI						
Total	40	8.63	1,094,800	6.57	5,590	5.51
REGION X						
AK						
ID						
OR	2	0.43	14,900	0.09	50	0.05
WA	4	0.86	18,058	0.11	129	0.13
Total	6	1.29	32,958	0.2	179	0.18
U.S. TOTAL	464	100.00	16,666,822	100.00	101,484	100.00

Source: Meta Systems Inc. calculations based on EPA Section 308 Survey data (1978 and 1979), and Economic Information Systems data (1979).

B. PLANT SIZES

Plant sizes are measured in terms of both pharmaceutical sales in 1979 and pharmaceutical employment. Measured either way, there are more small plants than large plants, as shown in Table IX-2. In terms of sales, plants tend to be concentrated at the small end of the scale. Nearly one-quarter of the plants had sales of less than $5 million, and over one-half had sales under $20 million. At the other end of the scale, there are 21 plants (5 percent) with sales between $200 and $499.9 million and only three plants (less than 1 percent) with sales of $500 million or more in 1979.

A similar distribution of sizes is found when plants are ranked according to number of pharmaceutical employment. Nearly one-third have less than 20 employees and about 60 percent have less than 100 employees. At the other end of the range, 53 plants (over 11 percent) have 500 or more employees.

TABLE IX-2

PLANT SIZES: SALES AND EMPLOYMENT

Sales ($ millions)	Number of Plants	Percent of Total
Less than 5	111	24
5-19.9	177	38
20-49.9	79	17
50-199.9	69	15
200-499.9	21	5
500 or greater	3	1
Missing data	4	1
Total	464	100
Number of Employees		
1-4	60	13
5-19	84	18
20-99	137	30
100-499	117	25
500-2499	47	10
2,500 or more	6	1
Missing data	13	3
Total	464	100

Source: Meta Systems, Inc., calculations based on EPA Section 308 survey data (1978 and 1979) and Economic Information Systems data (1979).

X. TREATMENT TECHNOLOGY AND COSTING

Control technologies for removing pollutants are customarily classified as in-plant and end-of-pipe. In-plant control includes source reduction and treatment technologies. Based on information presented in the Technical Support section of this document steam stripping is effective for removing volatile organic compounds (VOC) such as benzene, toluene, methylene chloride, and chloroform. These four VOCs are the compounds of concern in this preliminary assessment. One way to apply steam stripping is in-plant treatment before VOC-bearing waste streams mix with nonprocess wastewater, because the cost of steam stripping increases with wastewater flow. It is estimated that VOC-bearing wastewater is about 26 percent of the process wastewater reported in a previous 308 Survey (20). In addition, in-plant application of steam stripping will remove more and discharge less of the pollutant loadings than end-of-pipe application of steam stripping. Detailed study of plant specific conditions may show that treatments other than steam stripping are less expensive for some plants. But overall, in-plant treatment by steam stripping is applicable to most facilities, especially if stripped VOCs are reclaimed. In this preliminary analysis, the treatment technology addressed is steam stripping as an in-plant treatment.

The costs of steam stripping used in this analysis were derived using data from "Proposed Development Document for Effluent Limitations Guidelines and Standards for the Pharmaceutical Industry Point Source Category" [1] (5). Costs were developed on a plant-specific basis, using the 3-step process described below.

Step 1: Regression Analysis

In this step, regression analysis is used to estimate a relationship between treatment costs and wastewater flowrate. Information is obtained from the Development Document cited above for various flowrate sizes and costs.

Assumptions in the Analysis:

1. The steam stripping flowrate Q, is assumed to be 26 percent of the reported process wastewater flowrate. This is an engineering estimate that reflects the fact that 26 percent of the actual process flowrate contains priority pollutants and other pollutants of interest.

2. Influent concentration of pollutants has no effect on overall costs.

3. Annual costs are based on 300 days of plant operation.

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[1]This document was prepared for the regulatory analysis that supported the promulgation of Effluent Limitations, Guidelines, New Source Performance Standards, and Pretreatment Standards for the Pharmaceutical Industry.

The first regression estimates the relationship between capital costs (CC) and flowrate (Q). This analysis yields the equation used to compute CC for all plants for which process wastewater flow is known. The error term (E) is found to be negligible and hence is ignored in the analysis. The resultant equation is as follows:

$$Ln\ (CC) = [0.646\ Ln\ (Q) + 4.716 + E]$$

Where Q is in gallons/day and CC is in dollars.

Similarly, the second regression analysis yields the relationship between operating and maintenance costs (O&M) and Q. The equation is as follows:

$$Ln\ (O\&M) = [-0.224\ Ln\ (Q) + 4.658 + E]$$

Where Q is in gallons/day and O&M is in dollars/1000 gallons.

Step 2: Capital Costs Annualization

The annualized portion of capital costs is computed using a Capital Recovery Factor (CRF). The CRF is obtained by using the following equation:

$$CRF = [i(i+1)^n] / [(1+i)^n-1]$$

where i = interest rate = 10 percent
n = time period = 5 years
CRF = 0.26

Step 3: Annualized Costs Calculation

Annualized costs (AC) represent the sum of annualized capital costs, O&M and monitoring fee. Monitoring fee is the cost associated with sampling and analyzing VOCs concentration. While the Development Document cited above provides no data about the monitoring fee for this industry, the amount of $1,200 per year per plant is used here based on experience in other industries (such as Plastics Forming and Molding). Thus, the annualized costs are obtained using the equation:

$$AC = (CRF*CC) + MF + (O\&M)$$

where, MF = Monitoring Fee = $1,200/year

It is noted that the regression analysis performed on the O&M and Q yields an O&M cost per 1,000 gallons. This cost must be converted to an annual cost by multiplying the O&M cost by the wastewater flowrate in 300 days. With this conversion, the O&M costs are consistent with Capital Costs (CC).

To summarize, capital and O&M costs are estimated for each plant with wastewater flow, using the regression equations developed in Step 1. The capital costs are annualized using a CRF of 0.26.

Then the annual capital, O&M and monitoring costs are summed to obtain the annualized costs that are used in the economic impact analysis (Section XI). For example, the first plant in Table X-1 has a process wastewater flow of 8.316 mgd. Steam stripping applies to a flow of 2,162,160 gallons per day (8.326 mgd x 0.26). Substituting Q=2,162,160 gpd into the regression equations:

$$\text{Ln (CC)} = 0.646 \text{ Ln } (2{,}162{,}160) + 4.716 = 14.139$$
$$\text{or CC} = \$1{,}381{,}880$$

and

$$\text{Ln (O\&M)} = -0.224 \text{ Ln } (2{,}162{,}160) + 4.658 = 1.391$$
$$\text{or O\&M} = \$4.017/1000 \text{ gallons}$$

For the entire year, the O&M costs are:

$$4.017 \times (2{,}162{,}160/1000) \times 300 = \$2{,}605{,}781/\text{yr}$$

Thus annualized costs are:

$$(0.26 \times 1{,}381{,}880) + 2{,}605{,}781 + 1200 = \$2{,}971{,}521/\text{yr}$$

This estimate of annualized costs is shown in the last column of Table X-1.

For these 224 pharmaceutical plants, total annualized cost is $34.6 million and total capital cost is $21.7 million. Steam stripping is a relatively expensive treatment process to operate, with an annual O&M cost of $28.6 million for these 224 plants. For the 49 pharmaceutical plants that are direct dischargers, the total annualized costs is $13.8 million. For the 175 plants that are indirect dischargers, the total annualized cost is $20.8 million.

TABLE X-1

CALCULATION OF ANNUALIZED COSTS FOR PLANTS WITH PROCESS WASTEWATER FLOW
(Plants ordered by Annualized Cost)

Line No.	Process Wastewater Flow (mgd)	Capital Cost ($)	O&M Cost ($/yr)	Monitoring Fee ($/yr)	Annualized Cost ($)
1	8.3160	1,381,880	2,605,781	1200	2,971,521
2	2.9730	711,033	1,172,961	1200	1,361,731
3	2.0250	554,825	870,703	1200	1,018,266
4	1.8000	514,176	794,650	1200	931,489
5	1.7000	495,536	760,173	1200	892,096
6	1.6500	486,072	742,766	1200	872,191
7	1.6350	483,212	737,520	1200	866,192
8	1.4480	446,747	671,183	1200	790,235
9	1.3000	416,690	617,311	1200	728,434
10	1.2500	406,265	598,806	1200	707,179
11	1.1700	389,272	568,848	1200	672,738
12	1.1000	374,063	542,257	1200	642,135
13	1.0920	372,304	539,194	1200	638,608
14	1.0650	366,331	528,820	1200	626,658
15	1.0400	360,752	519,161	1200	615,528
16	1.0280	358,058	514,507	1200	610,162
17	1.0070	353,315	506,332	1200	600,736
18	0.9940	350,362	501,252	1200	594,878
19	0.9000	328,584	464,06#	1200	551,943
20	0.8780	323,372	455,235	1200	541,741
21	0.8500	316,672	443,929	1200	528,667
22	0.7780	299,074	414,462	1200	494,557
23	0.7400	289,554	398,665	1200	476,249
24	0.7010	279,601	382,262	1200	457,221
25	0.7000	279,344	381,839	1200	456,730
26	0.5270	232,539	306,344	1200	368,888
27	0.5000	224,771	294,093	1200	354,588
28	0.5000	224,771	294,093	1200	354,588
29	0.4640	214,179	277,525	1200	335,225
30	0.4300	203,904	261,611	1200	316,601
31	0.4250	202,369	259,247	1200	313,832
32	0.4100	197,726	252,118	1200	305,479
33	0.3870	190,488	241,073	1200	292,523
34	0.3800	188,255	237,682	1200	288,544
35	0.3800	188,255	237,682	1200	288,544
36	0.3620	182,445	228,898	1200	278,227
37	0.3500	178,515	222,988	1200	271,280
38	0.3500	178,515	222,988	1200	271,280
39	0.3400	175,203	218,028	1200	265,446
40	0.2950	159,849	195,284	1200	238,652

TABLE X-1 (continued)

CALCULATION OF ANNUALIZED COSTS FOR PLANTS WITH PROCESS WASTEWATER FLOW
(Plants ordered by Annualized Cost)

Line No.	Process Wastewater Flow (mgd)	Capital Cost ($)	O&M Cost ($/yr)	Monitoring Fee ($/yr)	Annualized Cost ($)
41	0.2820	155,262	188,572	1200	230,730
42	0.2820	155,262	188,572	1200	230,730
43	0.2820	155,262	188,572	1200	230,730
44	0.2770	153,478	185,972	1200	227,660
45	0.2600	147,326	177,053	1200	217,118
46	0.2590	146,959	176,524	1200	216,492
47	0.2400	139,901	166,390	1200	204,496
48	0.2320	136,871	162,070	1200	199,377
49	0.2230	133,417	157,170	1200	193,565
50	0.2170	131,087	153,878	1200	189,659
51	0.2100	128,339	150,012	1200	185,068
52	0.2000	124,357	144,439	1200	178,444
53	0.1900	120,304	138,802	1200	171,739
54	0.1830	117,422	134,818	1200	166,993
55	0.1800	116,175	133,099	1200	164,946
56	0.1740	113,658	129,643	1200	160,826
57	0.1700	111,963	127,325	1200	158,061
58	0.1660	110,254	124,994	1200	155,279
59	0.1660	110,254	124,994	1200	155,279
60	0.1610	108,097	122,062	1200	151,778
61	0.1600	107,663	121,473	1200	151,075
62	0.1400	98,765	109,517	1200	136,771
63	0.1400	98,765	109,517	1200	136,771
64	0.1300	94,148	103,396	1200	129,432
65	0.1270	92,739	101,540	1200	127,204
66	0.1250	91,793	100,297	1200	125,712
67	0.1250	91,793	100,297	1200	125,712
68	0.1250	91,793	100,297	1200	125,712
69	0.1180	88,438	95,910	1200	120,440
70	0.1100	84,517	90,825	1200	114,321
71	0.1070	83,021	88,897	1200	111,998
72	0.1070	83,021	88,897	1200	111,998
73	0.1040	81,510	86,957	1200	109,659
74	0.1010	79,983	85,004	1200	107,303
75	0.1010	79,983	85,004	1200	107,303
76	0.1000	79,470	84,350	1200	106,514
77	0.1000	79,470	84,350	1200	106,514
78	0.1000	79,470	84,350	1200	106,514
79	0.0900	74,241	77,728	1200	98,513

TABLE X-1 (continued)

CALCULATION OF ANNUALIZED COSTS FOR PLANTS WITH PROCESS WASTEWATER FLOW
(Plants ordered by Annualized Cost)

Line No.	Process Wastewater Flow (mgd)	Capital Cost ($)	O&M Cost ($/yr)	Monitoring Fee ($/yr)	Annualized Cost ($)
80	0.0900	74,241	77,728	1200	98,513
81	0.0890	73,707	77,057	1200	97,701
82	0.0880	73,171	76,384	1200	96,887
83	0.0850	71,550	74,356	1200	94,430
84	0.0800	68,802	70,939	1200	90,289
85	0.0800	68,802	70,939	1200	90,289
86	0.0790	68,245	70,249	1200	89,453
87	0.0760	66,560	68,170	1200	86,929
88	0.0750	65,993	67,473	1200	86,082
89	0.0640	59,566	59,660	1200	76,573
90	0.0640	59,566	59,660	1200	76,573
91	0.0630	58,963	58,935	1200	75,689
92	0.0600	57,134	56,745	1200	73,017
93	0.0600	57,134	56,745	1200	73,017
94	0.0590	56,517	56,010	1200	72,119
95	0.0560	54,643	53,787	1200	69,402
96	0.0530	52,734	51,537	1200	66,649
97	0.0520	52,089	50,781	1200	65,722
98	0.0520	52,089	50,781	1200	65,722
99	0.0490	50,127	48,493	1200	62,916
100	0.0470	48,796	46,950	1200	61,022
101	0.0450	47,444	45,392	1200	59,107
102	0.0440	46,760	44,607	1200	58,142
103	0.0420	45,376	43,025	1200	56,196
104	0.0420	45,376	43,025	1200	56,196
105	0.0400	43,968	41,427	1200	54,226
106	0.0400	43,968	41,427	1200	54,226
107	0.0400	43,968	41,427	1200	54,226
108	0.0390	43,255	40,621	1200	53,232
109	0.0380	42,535	39,810	1200	52,231
110	0.0370	41,808	38,995	1200	51,224
111	0.0370	41,808	38,995	1200	51,224
112	0.0370	41,808	38,995	1200	51,224
113	0.0370	41,808	38,995	1200	51,224
114	0.0360	41,075	38,175	1200	50,210
115	0.0350	40,334	37,349	1200	49,189
116	0.0340	39,586	36,518	1200	48,161
117	0.0340	39,586	36,518	1200	48,161
118	0.0340	39,586	36,518	1200	48,161

TABLE X-1 (continued)

CALCULATION OF ANNUALIZED COSTS FOR PLANTS WITH PROCESS WASTEWATER FLOW
(Plants ordered by Annualized Cost)

Line No.	Process Wastewater Flow (mgd)	Capital Cost ($)	O&M Cost ($/yr)	Monitoring Fee ($/yr)	Annualized Cost ($)
119	0.0340	39,586	36,518	1200	48,161
120	0.0340	39,586	36,518	1200	48,161
121	0.0330	38,830	35,682	1200	47,125
122	0.0330	38,830	35,682	1200	47,125
123	0.0320	38,066	34,840	1200	46,082
124	0.0310	37,293	33,992	1200	45,030
125	0.0290	32,000	32,278	1200	42,901
126	0.0290	35,720	32,278	1200	42,901
127	0.0260	33,287	29,655	1200	39,637
128	0.0250	32,454	28,766	1200	38,528
129	0.0250	32,454	28,766	1200	38,528
130	0.0230	30,753	26,964	1200	36,277
131	0.0230	30,753	26,964	1200	36,277
132	0.0220	29,882	26,050	1200	35,133
133	0.0200	28,098	24,193	1200	32,805
134	0.0200	28,098	24,193	1200	32,805
135	0.0200	28,098	24,193	1200	32,805
136	0.0200	28,098	24,193	1200	32,805
137	0.0190	27,182	23,249	1200	31,619
138	0.0180	26,249	22,293	1200	30,418
139	0.0180	26,249	22,293	1200	30,418
140	0.0170	25,297	21,326	1200	29,200
141	0.0170	25,297	21,326	1200	29,200
142	0.0160	24,326	20,346	1200	27,963
143	0.0150	23,332	19,352	1200	26,707
144	0.0140	22,315	18,343	1200	25,430
145	0.0130	21,272	17,318	1200	24,130
146	0.0120	20,200	16,275	1200	22,804
147	0.0110	19,096	15,213	1200	21,450
148	0.0100	17,956	14,128	1200	20,065
149	0.0100	17,956	14,128	1200	20,065
150	0.0100	17,956	14,128	1200	20,065
151	0.0100	17,956	14,128	1200	20,065
152	0.0100	17,956	14,128	1200	20,065
153	0.0100	17,956	14,128	1200	20,065
154	0.0100	17,956	14,128	1200	20,065
155	0.0090	16,774	13,019	1200	18,644
156	0.0090	16,774	13,019	1200	18,644
157	0.0090	16,774	13,019	1200	18,644
158	0 0080	15,545	11,882	1200	17,183

TABLE X-1 (continued)

CALCULATION OF ANNUALIZED COSTS FOR PLANTS WITH PROCESS WASTEWATER FLOW
(Plants ordered by Annualized Cost)

Line No.	Process Wastewater Flow (mgd)	Capital Cost ($)	O&M Cost ($/yr)	Monitoring Fee ($/yr)	Annualized Cost ($)
159	0.0080	15,545	11,882	1200	17,183
160	0.0080	15,545	11,882	1200	17,183
161	0.0080	15,545	11,882	1200	17,183
162	0.0070	14,261	10,712	1200	15,674
163	0.0070	14,261	10,712	1200	15,674
164	0.0060	12,909	9,050	1200	14,110
165	0.0060	12,909	9,505	1200	14,110
166	0.0050	11,475	8,251	1200	12,478
167	0.0050	11,475	8,251	1200	12,478
168	0.0050	11,475	8,251	1200	12,478
169	0.0050	11,475	8,251	1200	12,478
170	0.0050	11,475	8,251	1200	12,478
171	0.0050	11,475	8,251	1200	12,478
172	0.0040	9,934	6,939	1200	10,759
173	0.0040	9,934	6,939	1200	10,759
174	0.0040	9,934	6,939	1200	10,759
175	0.0040	9,934	6,939	1200	10,759
176	0.0040	9,934	6,939	1200	10,759
177	0.0040	9,934	6,939	1200	10,759
178	0.0040	9,934	6,939	1200	10,759
179	0.0030	8,249	5,550	1200	8,927
180	0.0030	8,249	5,550	1200	8,927
181	0.0030	8,249	5,550	1200	8,927
182	0.0030	8,249	5,550	1200	8,927
183	0.0030	8,249	5,550	1200	8,927
184	0.0030	8,249	5,550	1200	8,927
185	0.0020	6,348	4,052	1200	6,927
186	0.0020	6,348	4,052	1200	6,927
187	0.0020	6,348	4,052	1200	6,927
188	0.0020	6,348	4,052	1200	6,927
189	0.0020	6,348	4,052	1200	6,927
190	0.0020	6,348	4,052	1200	6,927
191	0.0020	6,348	4,052	1200	6,927
192	0.0020	6,348	4,052	1200	6,927
193	0.0020	6,348	4,052	1200	6,927
194	0.0020	6,348	4,052	1200	6,927
195	0.0020	6,348	4,052	1200	6,927
196	0.0020	6,348	4,052	1200	6,927
197	0.0010	4,057	2,366	1200	4,637
198	0.0010	4,057	2,366	1200	4,637

TABLE X-1 (continued)

CALCULATION OF ANNUALIZED COSTS FOR PLANTS WITH PROCESS WASTEWATER FLOW
(Plants ordered by Annualized Cost)

Line No.	Process Wastewater Flow (mgd)	Capital Cost ($)	O&M Cost ($/yr)	Monitoring Fee ($/yr)	Annualized Cost ($)
199	0.0010	4,057	2,366	1200	4,637
200	0.0010	4,057	2,366	1200	4,637
201	0.0010	4,057	2,366	1200	4,637
202	0.0010	4,057	2,366	1200	4,637
203	0.0010	4,057	2,366	1200	4,637
204	0.0010	4,057	2,366	1200	4,637
205	0.0010	4,057	2,366	1200	4,637
206	0.0010	4,057	2,366	1200	4,637
207	0.0010	4,057	2,366	1200	4,637
208	0.0010	4,057	2,366	1200	4,637
210	0.0010	4,057	2,366	1200	4,637
211	0.0010	4,057	2,366	1200	4,637
212	0.0010	4,057	2,366	1200	4,637
213	0.0010	4,057	2,366	1200	4,637
214	0.0010	4,057	2,366	1200	4,637
215	0.0010	4,057	2,366	1200	4,637
216	0.0010	4,057	2,366	1200	4,637
217	0.0010	4,057	2,366	1200	4,637
218	0.0010	4,057	2,366	1200	4,637
219	0.0010	4,057	2,366	1200	4,637
220	0.0010	4,057	2,366	1200	4,637
221	0.0010	4,057	2,366	1200	4,637
222	0.0010	4,057	2,366	1200	4,637
223	0.0010	4,057	2,366	1200	4,637
224	0.0003	1,864	930	1200	2,621
TOTAL	53.8463	21,745,960	28,608,532	267,600	34,612,716

Source: Meta Systems, Inc. calculations based on data from Agency reports

XI. ESTIMATED ECONOMIC IMPACTS

The Clean Water Act requires that effluent limitations be both technically and economically achievable. This section addresses the question of whether regulations to control the discharge of certain VOCs are economically achievable by comparing the estimated treatment costs for individual plants to their estimated sales and profits, as measures of the industry's ability to pay for treatment.

Compliance costs were estimated for all direct and indirect discharging plants for which flow data are available (i.e. 228 plants) according to the procedure discussed in Section X. Zero discharging plants are not included since they will not have additional treatment costs. Plant-specific impacts are measured in two ways: the ratio of annualized compliance costs to sales, and the reduction in profits resulting from the costs of compliance.

The cost to sales ratio gives a preliminary assessment of the relative impact of the regulation. If the ratio is small, then compliance costs are small in relation to sales and so the plant is likely to be able to carry these costs. The benchmarks that distinguish small impacts from large depend on profit levels in the industry. The second measure, reduction in profits, compares the compliance costs to the amount of funds available to pay these costs. Both of these measures are worst case calculations in the sense that they assume there will be no price increases to cover all or part of the cost increases.

Both impact measures require an estimate of plant-specific sales. Since sales data are not available for five of the plants, impacts are analyzed for 223 plants. These include 48 direct dischargers and 175 indirect dischargers. Plants are also classified according to their production processes. There are four basic production processes:

A) Fermentation
B) Biological Extraction
C) Chemical Synthesis
D) Formulation

Each plant has one or more of these processes, and subcategories are defined in terms of combinations of processes. All combinations of discharger status and subcategory are included in the analysis, except for subcategory AB. There is only one plant in subcategory AB, and it is an indirect discharger. It is not included in the analysis because flow data are not available for this plant. For many discharge/subcategory groups, all of the plants are analyzed. Table XI-1 presents a comparison of plants analyzed to existing plants.

TABLE XI-1

NUMBER OF PLANTS BY DISCHARGE STATUS AND SUBCATEGORIES:
ALL PLANTS AND PLANTS ANALYZED FOR IMPACTS

	Discharge Status				
	Direct Dischargers		Indirect Dischargers		
Subcat.	All Plants	Plants Analyzed	All Plants	Plants Analyzed	Zero Dischargers
A	2	2	2	1	0
AB	0	0	1	0	0
ABC	0	0	1	1	0
ABCD	1	1	7	6	0
ABD	0	0	4	3	0
AC	3	3	0	0	0
ACD	1	1	9	7	0
AD	1	1	4	4	0
B	2	2	16	12	4
BC	2	2	7	6	3
BCD	0	0	8	8	1
BD	3	3	17	10	2
C	13	10	23	19	11
CD	2	2	29	21	12
D	22	21	156	77	92
E	0	0	2	0	0
Unknown	0	0	0	0	1
Total	52	48	286	175	126

Source: Meta Systems, Inc. calculations, based on Section 308 survey data.

A. COMPLIANCE COST TO SALES RATIO

The first measure of impact is a comparison of each plant's annualized compliance cost to its sales, using estimates of costs and sales in 1979 dollars. The cost estimation procedures are described in Section X of this report. Sales estimates were provided by Economic Information Systems or were estimated by the Agency on the basis of plant employment and the sales at other plants.[2]

Table XI-2 lists the 228 plants in order of this cost to sales ratio expressed as a percent. The ratio could not be calculated for five of the plants (marked *), due to missing sales and employment data. Annualized compliance costs as a percentage of sales range from a high of 9.04 percent to a low of 0.01 percent. The median for all plants incurring costs is 0.15 percent. Therefore, compliance costs for most plants are estimated to be a very small proportion of their total revenues, even assuming that none of the costs are passed on to consumers in the form of higher prices. However, a number of plants will experience higher compliance costs. Thirteen plants, or 5.8 percent of the plants, are estimated to have annualized compliance costs equal to 2 percent or more of their sales, and 36 plants, or 16.1 percent of the plants, are estimated to have compliance costs equal to 1 percent or more of sales.

Since this preliminary analysis assumes that each plant will use the same pollution control option, regardless of discharge status or subcategory, treatment costs are simply a function of wastewater flow. Therefore, impacts were not analyzed to see if they differed among subcategories and/or discharge type.

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[2]These estimates were prepared for earlier analyses. For a description of the estimation procedures, see Appendix A: Estimation of Pharmaceutical Plant Sales, Economic Analysis of Effluent Standards and Limitations for the Pharmaceutical Industry, (21) EPA 440/2-83-013, September 1983.

TABLE XI-2

PLANTS BY DISCHARGE STATUS, SUBCATEGORY AND ANNUALIZED COMPLIANCE COSTS AS PERCENTAGE OF SALES

Plant	Discharge Status	Subcategory	Ratio of Annual Cost to Sales (Percent)
1	I	D	9.04
2	I	AD	6.91
3	I	BCD	5.03
4	D	C	3.42
5	D	AC	3.26
6	I	C	3.12
7	I	D	3.11
8	D	C	2.79
9	I	B	2.77
10	I	ACD	2.71
11	I	ACD	2.67
12	D	C	2.65
13	D	D	2.19
14	D	ABCD	1.85
15	DI	D	1.85
16	D	C	1.75
17	I	C	1.71
18	D	D	1.60
19	D	D	1.53
20	D	AC	1.51
21	D	B	1.48
22	I	C	1.40
23	D	CD	1.39
24	I	CD	1.38
25	D	A	1.35
26	D	AC	1.30
27	I	CD	1.20
28	I	BD	1.15
29	D	C	1.12
30	D	ACD	1.07
31	D	A	1.06
32	D	D	1.05
33	I	CD	1.03
34	I	B	1.02
35	D	C	1.02
36	I	CD	1.01
37	D	AD	0.94
38	I	C	0.94
39	I	BD	0.82
40	I	C	0.81

TABLE XI-2 (continued)

PLANTS BY DISCHARGE STATUS, SUBCATEGORY AND ANNUALIZED COMPLIANCE COSTS AS PERCENTAGE OF SALES

Plant	Discharge Status	Subcategory	Ratio of Annual Cost to Sales (Percent)
41	I	BC	0.79
42	I	C	0.75
43	I	ACD	0.73
44	D	D	0.72
45	I	C	0.70
46	I	BD	0.69
47	D	BD	0.68
48	D	C	0.60
49	D	D	0.59
50	I	D	0.55
51	I	D	0.53
52	I	D	0.51
53	D	D	0.50
54	I	D	0.47
55	I	D	0.45
56	I	D	0.45
57	I	B	0.44
58	I	AD	0.43
59	I	D	0.42
60	D	D	0.39
61	I	ABC	0.38
62	I	BCD	0.36
63	I	D	0.36
64	I	C	0.35
65	I	C	0.35
66	I	D	0.35
67	I	B	0.34
68	I	D	0.33
69	I	CD	0.33
70	D	BC	0.32
71	I	D	0.32
72	I	D	0.31
73	D	BD	0.31
74	I	BCD	0.31
75	I	C	0.31
76	I	CD	0.30
77	I	BCD	0.29
78	I	ABCD	0.29
79	I	C	0.28
80	I	B	0.27

TABLE XI-2 (continued)

PLANTS BY DISCHARGE STATUS, SUBCATEGORY AND ANNUALIZED COMPLIANCE COSTS AS PERCENTAGE OF SALES

Plant	Discharge Status	Subcategory	Ratio of Annual Cost to Sales (Percent)
81	I	ACD	0.25
82	I	D	0.25
83	I	CD	0.24
84	I	D	0.24
85	I	B	0.24
86	I	AD	0.23
87	I	CD	0.23
88	I	BD	0.23
89	I	B	0.22
90	I	D	0.21
91	D	BD	0.20
92	I	D	0.20
93	I	B	0.20
94	I	B	0.19
95	D	CD	0.19
96	D	BC	0.19
97	I	D	0.19
98	I	D	0.18
99	I	C	0.18
100	I	CD	0.18
101	I	ABCD	0.17
102	D	C	0.17
103	I	D	0.15
104	I	D	0.15
105	I	C	0.15
106	I	CD	0.15
107	I	BD	0.15
108	D	D	0.14
109	I	ABCD	0.14
110	D	D	0.14
111	I	D	0.14
112	I	CD	0.14
113	I	CD	0.14
114	I	D	0.13
115	I	D	0.13
116	I	CD	0.12
117	I	D	0.12
118	I	ABCD	0.12
119	I	AD	0.12
120	I	CD	0.12
121	I	D	0.12

TABLE XI-2 (continued)

PLANTS BY DISCHARGE STATUS, SUBCATEGORY AND ANNUALIZED COMPLIANCE COSTS AS PERCENTAGE OF SALES

Plant	Discharge Status	Subcategory	Ratio of Annual Cost to Sales (Percent)
122	I	ACD	0.12
123	D	D	0.11
124	I	D	0.11
125	I	BD	0.11
126	I	BC	0.11
127	I	D	0.10
128	I	ACD	0.10
129	I	BD	0.10
130	D	D	0.10
131	I	D	0.10
132	I	D	0.10
133	I	BD	0.10
134	I	C	0.10
135	I	D	0.10
136	I	B	0.10
137	I	ABCD	0.10
138	I	D	0.10
139	D	C	0.09
140	D	D	0.09
141	I	ABCD	0.08
142	I	D	0.08
143	I	D	0.08
144	I	D	0.08
145	I	D	0.08
146	I	D	0.08
147	I	D	0.08
148	D	D	0.07
149	D	D	0.07
150	I	D	0.07
151	I	D	0.07
152	DZ	D	0.07
153	I	D	0.07
154	I	D	0.07
155	I	D	0.07
156	I	D	0.07
157	I	B	0.07
158	I	CD	0.06
159	I	D	0.06
160	I	D	0.06
161	I	D	0.06

TABLE XI-2 (continued)

PLANTS BY DISCHARGE STATUS, SUBCATEGORY AND ANNUALIZED COMPLIANCE COSTS AS PERCENTAGE OF SALES

Plant	Discharge Status	Subcategory	Ratio of Annual Cost to Sales (Percent)
162	I	D	0.06
163	I	D	0.06
164	I	CD	0.06
165	I	ABD	0.06
166	I	D	0.06
167	I	BD	0.06
168	I	BC	0.06
169	I	D	0.06
170	I	CD	0.06
171	I	ABD	0.06
172	I	BCD	0.06
173	I	C	0.05
174	I	D	0.05
175	I	ACD	0.05
176	D	B	0.05
177	I	D	0.05
178	I	D	0.05
179	I	D	0.05
180	I	CD	0.05
181	I	C	0.05
182	I	BC	0.05
183	I	D	0.05
184	I	A	0.05
185	I	D	0.05
186	I	CD	0.04
187	D	C	0.04
188	I	C	0.04
189	D	D	0.04
190	I	D	0.04
191	I	D	0.04
192	I	BCD	0.04
193	I	BCD	0.04
194	I	CD	0.04
195	I	D	0.04
196	I	BD	0.03
197	I	D	0.03
198	I	C	0.03
199	I	D	0.03
200	I	D	0.03
201	I	BCD	0.03

TABLE XI-2 (continued)

PLANTS BY DISCHARGE STATUS, SUBCATEGORY AND ANNUALIZED COMPLIANCE COSTS AS PERCENTAGE OF SALES

Plant	Discharge Status	Subcategory	Ratio of Annual Cost to Sales (Percent)
202	I	B	0.03
203	I	D	0.03
204	D	D	0.03
205	I	BC	0.03
206	I	D	0.03
207	I	D	0.03
208	D	D	0.02
209	ID	D	0.02
210	I	D	0.02
211	I	D	0.02
212	I	BC	0.02
213	D	D	0.02
214	I	ABD	0.02
215	I	CD	0.02
216	I	D	0.02
217	I	D	0.02
218	I	D	0.01
219	I	D	0.01
220	I	C	0.01
221	I	D	0.01
222	I	D	0.01
223	I	D	0.01
224	D	C	*
225	I	D	*
226	D	C	*
227	D	C	*
228	D	D	*

NOTE:

Discharge Status: I = Indirect Discharge
D = Direct Discharge
Z = Zero Discharge

Subcategory: A = Fermentation
B = Biological Extraction
C = Chemical Synthesis
D = Packaging
* = Insufficient Data

Source: Meta Systems, Inc. calculations based on EPA data.

B. CHANGE IN PROFITS

The second measure of regulatory impact estimates the change in profitability resulting from treatment compliance costs. Since operating cost data for individual plants are not available at this time, plant-level profits are estimated using company and industry profitability rates. The approach requires four steps.

1. Plant profits without the regulation are estimated by multiplying plant sales by the appropriate ratio of profits before taxes to sales. Plant sales are described above and profit ratios are discussed below.

2. Annualized compliance costs are subtracted from profits to estimate plant profits with the regulation.

3. A new profit rate is calculated as the ratio of profits with the regulation to sales. Both steps 2 and 3 assume the plant is unable to pass on any of the compliance costs in the form of higher prices. By using profits before taxes, it is not necessary to calculate the impact on tax payments resulting from compliance costs.

4. Impact is measured as the change in profitability rate due to compliance costs.

Two sources of profitability rate data are used in this exercise. Average before-tax profits to sales ratios are calculated for each of the 43 companies for which income account data were collected. (See the discussion in Section IX, dealing with financial ratios.) The company's profitability rate is used for each plant owned by the company. For plants not owned by one of these 43 companies, the ratio of pharmaceutical before-tax profits to sales, as published by Robert Morris Associates, is used. This ratio is 6.1 percent.

The impacts on profits are presented in Table XI-3. This table lists the 223 plants analyzed, ordered by the percentage change in profits resulting from the compliance costs. The table also presents the plant's estimated profit rates without compliance costs, and with compliance costs. For example, the profits for the 25th plant on the list decline from 6.10 percent to 4.95 percent, which is an 18.91 percent decline in their profits. Profit changes range from a low of 0.08 percent to a high of 148.14 percent. The two plants with the greatest declines in profits both have negative profits after paying compliance costs, and thus declines in profits exceed 100 percent. The median decline is 2.11 percent, as in a decline in profit rates from 6.10 percent to 5.97 percent. The impact on the majority of plants with costs is very small. However, 44 plants, or 19.7 percent, have a decline in profits of 10 percent or more. For example, a 10 percent decline would lower a 7.85 percent profit rate to 7.06 percent, or a profit rate of 4.84 percent to 4.34 percent.

XI-3

EFFECT OF REGULATION ON PROFITS

Plant	Profit As Percentage of Sales		Percentage Change in Profits
	Without Regulation	With Regulation	
1	6.10	-2.94	-148.14
2	6.10	-0.81	-113.32
3	6.10	1.07	-82.50
4	6.10	2.68	-56.05
5	6.10	2.84	-53.36
6	6.10	2.98	-51.19
7	6.10	3.31	-45.81
8	6.10	3.33	-45.47
9	6.10	3.39	-44.40
10	6.10	3.43	-43.85
11	6.10	3.45	-43.51
12	6.10	3.91	-35.85
13	6.10	4.25	-30.37
14	6.10	4.25	-30.30
15	6.10	4.35	-28.75
16	6.10	4.39	-28.00
17	6.10	4.50	-26.28
18	6.10	4.57	-25.10
19	6.10	4.59	-24.77
20	6.10	4.62	-24.34
21	6.10	4.70	-22.95
22	6.10	4.72	-22.58
23	6.10	4.75	-22.10
24	6.10	4.80	-21.33
25	6.10	4.95	-18.91
26	6.10	4.98	-18.36
27	0.17	0.14	-18.06
28	6.10	5.03	-17.60
29	6.10	5.04	-17.36
30	6.13	5.08	-17.19
31	4.73	3.92	-17.10
32	6.10	5.07	-16.86
33	6.10	5.08	-16.77
34	6.10	5.08	-16.74
35	6.10	5.09	-16.58

XI-3 (continued)

EFFECT OF REGULATION ON PROFITS

Plant	Profit As Percentage of Sales: Without Regulation	Profit As Percentage of Sales: With Regulation	Percentage Change in Profits
36	19.84	16.73	-15.67
37	6.10	5.16	-15.48
38	6.10	5.16	-15.35
39	6.10	5.28	-13.52
40	6.10	5.35	-12.33
41	6.10	5.37	-11.97
42	6.10	5.40	-11.47
43	6.10	5.41	-11.36
44	6.10	5.42	-11.15
45	6.10	5.50	-9.87
46	14.31	12.92	-9.69
47	7.78	7.06	-9.23
48	6.10	5.55	-9.08
49	6.10	5.57	-8.73
50	6.10	5.59	-8.38
51	6.10	5.65	-7.44
52	6.10	5.68	-6.93
53	6.10	5.71	-6.40
54	6.10	5.72	-6.22
55	6.10	5.74	-5.98
56	8.41	7.91	-5.97
57	10.10	9.51	-5.84
58	4.60	4.33	-5.79
59	6.10	5.75	-5.75
60	6.10	5.75	-5.70
61	6.10	5.76	-5.55
62	14.31	13.52	-5.50
63	6.10	5.77	-5.47
64	6.10	5.77	-5.42
65	6.10	5.78	-5.28
66	6.10	5.78	-5.21
67	6.10	5.79	-5.09
68	6.10	5.79	-5.07
69	6.10	5.79	-5.03
70	6.10	5.79	-5.01
71	24.55	23.35	-4.90
72	6.10	5.80	-4.88
73	6.10	5.81	-4.83
74	6.10	5.81	-4.72
75	6.10	5.82	-4.61
76	7.78	7.43	-4.52
77	6.10	5.85	-4.17

XI-3 (continued)

EFFECT OF REGULATION ON PROFITS

Plant	Profit As Percentage of Sales: Without Regulation	Profit As Percentage of Sales: With Regulation	Percentage Change in Profits
78	6.10	5.86	-3.87
79	6.10	5.87	-3.79
80	6.10	5.87	-3.78
81	6.10	5.87	-3.70
82	12.70	12.25	-3.58
83	6.10	5.89	-3.46
84	6.10	5.90	-3.36
85	6.10	5.90	-3.33
86	6.10	5.90	-3.30
87	6.10	5.91	-3.20
88	6.10	5.91	-3.15
89	6.10	5.91	-3.09
90	6.10	5.92	-2.97
91	6.10	5.92	-2.92
92	7.78	7.56	-2.89
93	4.40	4.28	-2.80
94	6.10	5.93	-2.77
95	6.10	5.93	-2.75
96	14.31	13.95	-2.54
97	6.10	5.95	-2.54
98	6.10	5.95	-2.53
99	6.10	5.95	-2.51
100	6.10	5.95	-2.50
101	6.10	5.96	-2.37
102	19.84	19.37	-2.37
103	6.10	5.96	-2.37
104	6.13	5.99	-2.34
105	6.10	5.96	-2.31
106	6.10	5.96	-2.27
107	8.41	8.22	-2.24
108	19.84	19.40	-2.20
109	7.04	6.89	-2.19
110	6.10	5.97	-2.17
111	19.84	19.41	-2.15
112	6.10	5.97	-2.11
113	6.10	5.98	-2.02
114	6.10	5.98	-2.00
115	6.10	5.98	-1.96
116	6.10	5.98	-1.95
117	6.10	5.98	-1.90
118	6.10	5.99	-1.85
119	6.10	5.99	-1.82

XI-3 (continued)

EFFECT OF REGULATION ON PROFITS

Plant	Profit As Percentage of Sales: Without Regulation	Profit As Percentage of Sales: With Regulation	Percentage Change in Profits
120	13.73	13.48	-1.80
121	6.10	5.99	-1.75
122	6.10	6.00	-1.72
123	2.05	2.02	-1.69
124	6.10	6.00	-1.69
125	6.10	6.00	-1.66
126	6.10	6.00	-1.66
127	14.31	14.07	-1.66
128	6.10	6.00	-1.65
129	14.31	14.07	-1.65
130	6.10	6.00	-1.64
131	6.13	6.03	-1.64
132	6.10	6.00	-1.63
133	6.10	6.00	-1.62
134	6.10	6.01	-1.52
135	6.10	6.01	-1.46
136	6.10	6.02	-1.38
137	6.10	6.02	-1.37
138	6.10	6.02	-1.33
139	6.10	6.02	-1.23
140	6.10	6.03	
141	14.57	14.39	-1.22
142	6.10	6.03	-1.22
143	6.10	6.03	-1.20
144	6.10	6.03	-1.20
145	6.10	6.03	-1.18
146	6.10	6.03	-1.16
147	6.10	6.03	-1.14
148	6.13	6.06	-1.07
149	6.10	6.04	-1.07
150	6.10	6.04	-1.05
151	6.10	6.04	-1.04
152	6.10	6.04	-1.03
153	6.10	6.04	-1.03
154	6.10	6.04	-1.03
155	6.10	6.04	-1.02
156	6.10	6.04	-1.02
157	14.03	13.89	-0.98
158	6.10	6.04	-0.98
159	6.10	6.04	-0.98
160	6.10	6.04	-0.96
161	6.10	6.04	-0.95

XI-3 (continued)

EFFECT OF REGULATION ON PROFITS

Plant	Profit As Percentage of Sales: Without Regulation	Profit As Percentage of Sales: With Regulation	Percentage Change in Profits
162	11.83	11.72	-0.94
163	6.10	6.04	-0.92
164	6.10	6.05	-0.87
165	6.10	6.05	-0.85
166	6.10	6.05	-0.85
167	4.89	4.85	-0.82
168	6.13	6.08	-0.82
169	6.10	6.05	-0.82
170	6.10	6.05	-0.78
171	6.10	6.05	-0.78
172	12.31	12.21	-0.77
173	6.10	6.05	-0.76
174	7.78	7.72	-0.76
175	6.10	6.05	-0.75
176	6.10	6.05	-0.75
177	6.10	6.05	-0.75
178	6.10	6.06	-0.69
179	6.10	6.06	-0.68
180	14.31	14.21	-0.67
181	6.10	6.06	-0.67
182	6.10	6.06	-0.66
183	6.10	6.06	-0.64
184	6.10	6.06	-0.63
185	6.10	6.06	-0.62
186	6.10	6.06	-0.60
187	19.84	19.72	-0.60
188	6.10	6.06	-0.58
189	6.10	6.07	-0.57
190	6.10	6.07	-0.56
191	14.31	14.23	-0.55
192	6.10	6.07	-0.52
193	6.10	6.07	-0.51
194	6.10	6.07	-0.50
195	6.10	6.07	-0.49
196	19.84	19.74	-0.48
197	6.10	6.07	-0.48
198	17.99	17.91	-0.46
199	6.10	6.07	-0.42
200	20.00	19.93	-0.37
201	6.10	6.08	-0.36
202	6.10	6.08	-0.36
203	14.31	14.26	-0.35

XI-3 (continued)

EFFECT OF REGULATION ON PROFITS

Plant	Profit As Percentage of Sales: Without Regulation	Profit As Percentage of Sales: With Regulation	Percentage Change in Profits
204	19.84	19.77	-0.34
205	6.10	6.08	-0.33
206	24.00	23.92	-0.32
207	7.78	7.76	-0.32
208	6.10	6.08	-0.32
209	7.78	7.76	-0.31
210	6.10	6.08	-0.27
211	6.10	6.08	-0.27
212	7.78	7.76	-0.26
213	22.53	22.47	-0.25
214	19.84	19.79	-0.25
215	6.10	6.09	-0.23
216	18.07	18.04	-0.19
217	6.10	6.09	-0.17
218	6.10	6.09	-0.14
219	6.10	6.09	-0.13
220	19.01	18.98	-0.13
221	14.31	14.29	-0.13
222	7.78	7.77	-0.09
223	14.31	14.30	-0.08

Source: Meta Systems, Inc. calculations based on data obtained from EPA and Compustat Services, Inc.

C. CONCLUSIONS

Both of the impact measures support the conclusion that pharmaceutical manufacturing is generally a healthy industry and most plants would experience little or no impact from the compliance costs associated with regulating VOCs. The median profit rate without additional compliance costs is estimated to be 6.10 percent, and the median profit rate with compliance costs is estimated to be 6.00 percent, a decline of 1.6 percent. In terms of the ratio of compliance costs to sales, the median is 0.15 percent; and 187 plants out of the 223 analyzed have cost to sales ratios of 1 percent or less. However, some plants may experience significant impacts from this level of compliance costs. For 44 plants, out of the 223 analyzed, profits are estimated to fall by 10 percent or more due to this level of compliance costs. Likewise, 13 plants, out of the 223 analyzed, are estimated to have ratios of compliance costs to sales of 2 percent or more. The 44 plants with the largest estimated declines in profit include the 13 plants with the largest cost to sales ratios.

This analysis is intended to provide a general assessment of the potential impact of regulating VOCs. A more comprehensive analysis would include additional data and more precise impact measures. For example, this analysis was conducted using sales for 1979 and compliance cost estimates in 1979 dollars. Current plant-level sales data would reflect any changes in product mix and price changes that have taken place since 1979. Likewise, the financial ability of the plant to handle compliance costs could be better measured if plant-specific operating costs were available. For many plants in this analysis, an industry-wide profit rate was used. Additional and more current data would refine the assessments presented here. However, it is expected that the general conclusion, that these compliance costs are affordable for most plants, would be supported.

ENVIRONMENTAL IMPACT ANALYSIS

XII ENVIRONMENTAL IMPACT ANALYSIS

The environmental impact analysis summarizes the environmental considerations for the pharmaceutical manufacturing industry. The environmental considerations include an industry profile, projected and monitored human health and aquatic life impacts, as well as pollutant effect levels and environmental factors. This section is composed of three parts, a description of the methodology used in the analysis, a list of the data sources, and a summary of the environmental impacts.

A. METHODOLOGY

The environmental impacts of both direct and indirect discharging pharmaceutical manufacturing facilities were projected using a simplified dilution analysis. In addition, the impacts of monitored discharges from 47 direct and indirect discharging facilities were also evaluated.

1. Assumptions The following assumptions were used in the analysis:

- Industry-wide average pollutant concentrations were used to project instream concentrations.
- Background concentrations for each pollutant at the POTW and in the receiving streams were equal to zero.
- Complete mixing of the discharge flow and stream flow occurs across the stream at the discharge point.
- The plant's process water and water discharged to the POTW were obtained from a source other than the receiving stream.
- Removal efficiency rates were based on removals expected for a well-operated POTW with secondary treatment.
- Pollutant fate processes (e.g., sediment adsorption, volatilization, hydrolysis) were not considered. This results in environmentally conservative (higher) instream concentrations.

2. Projected Impacts of Direct Dischargers A simplified dilution analysis was performed for 22 of the 29 direct discharging pharmaceutical facilities in subcategories A, B, and C (Appendix N). Using industry-wide average pollutant concentrations, instream concentrations were projected at current treatment discharge levels and under low receiving stream flow conditions (Equation 1).

Equation 1

$$\text{Instream Pollutant Concentration (ug/l)} = \frac{\text{Plant Concentration (ug/l)} \times \text{Plant Flow (MGD)}}{\text{Plant Flow (MGD)} + \text{Stream Flow (MGD)}}$$

Instream pollutant concentrations were compared to EPA water quality criteria or toxic effect levels (reported in the MDSD's Toxics Data Base). Water quality criteria exceedances were determined by dividing the projected instream pollutant concentrations by the EPA water quality criteria or toxic effect levels (except for acute aquatic life criteria, which were compared directly to effluent levels). A value greater than one indicated an exceedance.

3. Projected Impacts of Indirect Dischargers The environmental impact on 26 POTWs and their receiving streams for 28 of the 130 indirect discharging pharmaceutical facilities (in subcategories A, B, and C) were also evaluated. A simplified POTW model and stream dilution analysis were used to project receiving stream impacts (Appendix O). POTW influent and effluent concentrations are shown in Equations 2 and 3.

Equation 2

$$\text{POTW Influent Concentration (ug/l)} = \text{Plant Concentration (ug/l)} \times \frac{\text{Plant Flow (MGD)}}{\text{Plant Flow (MGD)} + \text{POTW Flow (MGD)}}$$

Equation 3

$$\text{POTW Effluent Concentration (ug/l)} = \text{POTW Influent (ug/l)} \times (1 - \text{Treatment Removal Efficiency})$$

The simplified dilution model predicts the instream pollutant concentrations resulting from indirect discharging facilities (Equation 4).

Equation 4

$$\text{Instream Pollutant Concentration (ug/l)} = \frac{\text{POTW Effluent Concentration (ug/l)} \times \text{POTW Flow (MGD)}}{\text{POTW Flow (MGD)} + \text{Receiving Stream Flow (MGD)}}$$

Impacts on POTW operations were calculated in terms of inhibition of POTW processes and contamination of POTW sludges. Inhibition of POTW processes were determined by comparing calculated POTW influent levels (Equation 2) with inhibition levels, which were available for 12 volatile pollutants. Sludge contamination could not be evaluated as no values for sludge contamination for the volatiles have been published. For pharmaceutical facilities that discharge to the same POTW, their individual flows were summed prior to calculating the POTW influent and effluent concentrations.

4. Monitored Impacts of Direct and Indirect Dischargers The environmental impacts of current loadings, as monitored on 22 streams receiving direct discharges from pharmaceutical facilities and on 25 streams receiving discharges from pharmaceutical facilities discharging to POTWs, were also evaluated. Impacts of volatile pollutant loadings were assessed by comparing ambient

instream pollutant concentrations in STORET to EPA water quality criteria or toxic effect levels (reported in MDSD's Toxics Data Base). Data were retrieved from 1980 to present and summarized as detected (unremarked, nonzero data) or not detected (remarked, zero data) according to media type. Pollutant data for pharmaceutical facilities in the Permit Compliance System (PCS) with monitoring requirements or limitations were also summarized.

B. DATA SOURCES

The pharmaceutical manufacturing industry includes a total of 52 direct discharging facilities (29 in subcategories A, B, & C and 23 in subcategory D) and 285 indirect discharging facilities (130 in subcategories A, B & C and 155 in subcategory D) located throughout the United States and Puerto Rico.

Preliminary plant and stream information was readily available and sufficient to evaluate some of the direct and indirect discharging facilities in subcategories A, B, and C only. Based on initial review of available data by EPA, it was apparent that volatile organic compounds used as process solvents were likely to be the pollutants of concern. Therefore, the following environmental analysis focuses on these facilities and pollutants.

1. Plant-Specific Data Projected pharmaceutical plant and POTW effluent flows and projected plant pollutant loadings (Appendix P) were obtained from EPA's Industrial Technology Division (ITD) in October 1987. The locations of facilities and POTWs on receiving streams were obtained from the Industrial Facilities Discharge (IFD) data base (Appendix Q). (It should be noted that the names of the POTWs were matched as well as possible with the information in IFD; however, some POTWs may have been incorrectly identified.) The USGS cataloging and stream segment (reach) numbers, obtained from IFD, were used to obtain the receiving stream flow data from the W.E. Gates study. The W.E. Gates study contains calculated average and low flow statistics based on the best available flow data and on drainage areas for reaches throughout the United States.

2. POTW Evaluations POTW treatment efficiency removal rates were developed from POTW removal data and pilot plant studies (Appendix R). The removal rates assumed that the evaluated POTWs were well-operated and had at least secondary treatment in place.

Inhibition values were obtained from data published in the Federal Guidelines, State and Local Pretreatment Programs, January 1977 (EPA 430/9-76-017a) (Appendix O). No sludge contamination values were available for this analysis.

3. Monitoring Data Water quality data were obtained from the STORET Water Quality File (March 1988). Facility monitoring or limitations data were obtained from the Permit Compliance System (March 1988).

4. Water Quality Criteria (WQC) The ambient criteria for the protection of aquatic life and human health considerations were obtained from EPA criteria documents. Toxic effect levels (reported in the MDSD's Toxics Data Base) were used when criteria values were not available (Appendix S).

a. Aquatic Life. Several WQC values have been established for the protection of freshwater aquatic life (acute and chronic criteria). The acute value represents a maximum allowable 1-hour average concentration of a pollutant at any time and can be related to acute toxic effects on aquatic life. The chronic value represents the average allowable concentration, over a 4-day period, of a toxic pollutant and can be related to chronic effects resulting from long-term exposure to aquatic life. Freshwater criteria were used since the facilities evaluated discharge to freshwater rivers and streams.

b. Human Health Criteria. EPA established water quality criteria values to protect human health in terms of a pollutant's toxic effects and carcinogenic potential. These WQC values have been developed for two exposure routes: (1) ingesting the pollutant both through water and contaminated aquatic organisms, and (2) ingesting the pollutant through contamination of aquatic organisms only. The values for ingesting water and organisms were derived by assuming a daily ingestion of two liters of water and 6.5 grams of potentially contaminated fish products. Carcinogenicity values were used to access the potential effects on human health when a pollutant was suspected of being carcinogenic to humans.

Criteria for suspected or actual carcinogens have been developed in terms of three lifetime risks (risk levels of 10^{-5}, 10^{-6}, and 10^{-7}. Criteria at a risk level of 10^{-6} were chosen for this analysis. This risk level indicates a probability of one additional case of cancer for every 1,000,000 persons exposed. Toxic effects criteria for noncarcinogens are based on bodily disfunction, such as damage to the liver.

C. SUMMARY OF ENVIRONMENTAL IMPACTS

Receiving stream impacts were evaluated for 22 direct and 28 indirect pharmaceutical facilities in subcategories A, B, and C.

1. Projected Impacts of Direct Discharging Facilities A total of 22 direct facilities discharging 15 volatile organics to 22 stream segments were evaluated. At low receiving stream flow, pollutant instream concentrations were projected to exceed human health (water and organisms) criteria in 86 percent (19 of the total 22) of the receiving stream segments at current conditions (Table XII-1). A total of 8 pollutants (all known or suspected carcinogens) were projected to exceed water quality criteria using a target risk level of 10^{-6} for the carcinogens (Tables XII-1 and XII-2).

None of the volatile pollutants were projected to exceed aquatic life criteria or toxic effect levels (Tables XII-1 and XII-2).

2. Monitored Impacts of Direct Discharging Facilities Five of the 22 streams receiving discharges from 22 facilities were monitored for volatile pollutants (Table XII-3). Nine of the 15 evaluated pollutants were detected in water, tissue, or sediments in four of the five stream segments (Tables XII-3 and XII-4). Two of the pollutants exceed human health criteria in three of the five stream segments using a target risk level of 10^{-6} for the carcinogens (Table XII-3 and XII-4). None of the volatile pollutants exceed aquatic life criteria or aquatic life toxic effect levels. In addition, eleven of the evaluated pollutants were monitored or limited for 36 percent of the facilities in PCS (8 of 22) (Tables XII-3 and XII-4).

3. Projected Impacts of Indirect Discharging Facilities Receiving stream impacts were evaluated for 26 POTWs receiving discharges of 28 indirect pharmaceutical facilities. A total of 21 volatile pollutants discharging to 25 receiving streams were evaluated. At low receiving stream flow, pollutant instream concentrations were projected to exceed human health (water and organisms) criteria in 60 percent (15 of the total 25) of the receiving stream segments at current conditions (Table XII-5). Six pollutants (all known or suspected carcinogens) were projected to exceed water quality criteria using a target risk level of 10^{-6} for the carcinogens (Tables XII-5 and XII-6). None of the volatile pollutants were projected to exceed aquatic life criteria or toxic effect levels (Tables XII-5 and XII-6).

Impacts to POTW operations were also evaluated. At current conditions, no inhibition of POTW treatment processes is projected for the 12 volatile pollutants which have inhibition values. Sludge contamination could not be evaluated as no values for sludge contamination from volatile pollutants have been published.

TABLE XII-1

SUMMARY OF VOLATILE ORGANICS AND RECEIVING STREAMS WITH PROJECTED HUMAN HEALTH AND AQUATIC LIFE IMPACTS AT LOW FLOW UNDER CURRENT CONDITIONS
DIRECT DISCHARGERS (Subcategory A, B, and C)

	Projected Discharge of Pollutants	Known or Suspected Carcinogen	Human Health or Aquatic Life Criteria Available*	Pollutants Evaluated	Receiving Streams Evaluated	Percent of Receiving Streams with Exceedances Number	Pollutants Projected To Exceed Criteria
Human Health Impacts							
Volatile Organics	24	16**	22	15	22	86 (19/22)	8[a]
Aquatic Life Impacts (Chronic)							
Volatile Organics	24	--	21	14	22	0	0

NOTE: Projections were based on simplified dilution analysis assuming industry-wide average pollutant concentrations.
C = Carcinogen, M = Mutagen, T = Teratogen

*Criteria or toxic effect levels were available or estimated. Human health criteria (water and organisms) at a risk level of 10^{-6} for carcinogens.

**Criterion for halomethanes has been derived for an entire class of compounds. EPA does not state that each chemical in the class is a carcinogen.

[a]All known or suspected carcinogens.

TABLE XII-2

SUMMARY OF VOLATILE ORGANICS PROJECTED TO EXCEED CRITERIA AT LOW FLOW UNDER CURRENT CONDITIONS DIRECT DISCHARGERS (Subcategory A, B, and C)

Pollutant	Average Effluent Pollutant Concentration (µg/ℓ)	Water Quality Criteria[a] (µg/ℓ) Human Health (W&O)	Aquatic Life (Chronic)	Number of Exceedances Human Health (W&O)	Aquatic Life (Chronic)	Known or Suspected Effects
Volatile Organics[b]						
Benzene	94.8	0.66	265	10	--	C(A)/T
Bromodichloromethane	1.3	0.19	---	4	--	C
Chloroform	63.2	0.19	1,240	12	--	$C(B_2)/M$
Chloromethane	52.1	0.19	27,500	11	--	C(NIOSH-X)
1,2-Dichloroethane	83.7	0.94	20,000	7	--	$C(B_2)/M$
1,1-Dichloroehtene	90.0	0.033	2,400	19	--	C(C)
Methylene chloride	631.7	0.19	9,650	19	--	$C(B_2)$
Tetrachloromethane	25.3	0.4	352	7	--	$C(B_2)M$

NOTE:

Total No. of Facilities - 22
Total No. of Receiving Streams - 22
[a] For pollutants without EPA criteria, toxic effect levels, reported in the MDSD's Toxics Data Base or estimated using environmental factors, were used.
[b] Criterion for halomethanes has been derived for an entire class of compounds. EPA does not state that each chemical in the class is a carcinogen.
W&O = Ingesting water and organisms.
C = Carcinogen (CAG designation, if available, or other specified group designation).
M = Mutagen, T = Teratogen
CAG - A = Human carcinogen
B_2 = Probable human carcinogen
C = Possible human carcinogen
NIOSH - x = Potential carcinogen

TABLE XII-3

SUMMARY OF MONITORED RECEIVING STREAM IMPACTS
DIRECT AND INDIRECT DISCHARGERS (Subcategory A, B, and C)

Type of Discharge	Facilities Evaluated			Receiving Streams Evaluated		Pollutants Evaluated		Receiving Streams Monitored	Detected Pollutants	Receiving Streams with Detected Pollutants	Receiving Streams with Pollutants Exceeding Criteria[a]	Facilities with Monitoring Requirements or Limitations
Direct	22	22	15	5	9	4	3	8				
Indirect[b]	26-POTWs			25	21	6	8	4	3	5		
	28-Facilites											

NOTE: Receiving stream water quality data was obtained from STORET, 1980 to present (March 1988).
Facility information was obtained from the Permit Compliance System (March 1988).

[a] Human health criteria (water and organisms) at a risk level of 10^{-6} for carcinogens.
[b] 28 Facilities discharging to 26 POTWs.

TABLE XII-4

SUMMARY OF MONITORED POLLUTANT IMPACTS
DIRECT DISCHARGERS (Subcategory A, B, and C)

Pollutant	Number of Facilities in PCS[a]	Observations in Storet[b] Detected	Not Detected	Known or Suspected Effects[c]
Acrolein			W, S, T	
Benzene	4	W*, T	S	C(A)/T
Bromodichloromethane	2		W, S, T	C
Chloroform	5	W*	S, T	C(B2)/M
Chloromethane	1	T	W, S	C(NIOSH-X)
Dibromochlormethane	2		W, S, T	C
1,2-Dichloroethane	2		W, S, T	C(B2)/M
1,1-Dichloroehtene	1		W, S, T	C(C)
Ethylbenzene		T	W, S	
Methylene Chloride	4	T	W, S	C(B2)
Tetrachloroethene		W	S, T	C(B2)
Tetrachloromethane	1		W, S, T	C(B2)/M
Toluene	2	T	W, S	
1,1,1-Trichloroethane	1	W	S, T	
Trichloroethene		W	S, T	C(B2)/M

NOTE:

[a] Pharmaceutical facilities with monitoring or limits data in the Permit Compliance System (March 1988).

[b] STORET data 1980 to present. Detected = Unremarked or nonzero data. Not Detected = Remarked or zero data. Information is reported for the following sample media: S = Sediment, W = Water, and T = Tissue.

[c] Criterion for halomethanes has been derived for an entire class of compounds. EPA does not state that each chemical in the class is a carcinogen.

* Exceeds human health criteria for ingesting water and organisms (R = 1E-6).

C = Carcinogen (CAG designation, if available, or other specified group designation).
M = Mutagen, T = Teratogen

CAG - A = Human carcinogen
B2 = Probable human carcinogen
C = Possible human carcinogen
NIOSH-X = Potential carcinogen

TABLE XII-5

SUMMARY OF VOLATILE ORGANICS AND RECEIVING STREAMS WITH PROJECTED HUMAN HEALTH AND AQUATIC LIFE IMPACTS AT LOW FLOW UNDER CURRENT CONDITIONS
INDIRECT DISCHARGERS (Subcategory A, B, and C)

	Projected Discharge of Pollutants	Known or Suspected Carcinogen	Human Health or Aquatic Life Criteria Available*	Pollutants Evaluated	Receiving Streams Evaluated	Percent of Receiving Streams with Exceedances Number	Pollutants Projected To Exceed Criteria
HUMAN HEALTH IMPACTS							
Volatile Organics	24	16**	22	21	25	60 (15/25)	6[a]
AQUATIC LIFE IMPACTS (CHRONIC)							
Volatile Organics	24	--	21	21	25	0	0

NOTE: Projections were based on simplified dilution analysis assuming industry-wide average pollutant concentrations.
C = Carcinogen, M = Mutagen, T = Teratogen
*Criteria or toxic effect levels were available or estimated. Human health criteria (water and organisms) at a risk level of 10^{-6} for carcinogens.
**Criterion for halomethanes has been derived for an entire class of compounds. EPA does not state that each chemical in the class is a carcinogen.
[a]All known or suspected carcinogens.

TABLE XII-6

SUMMARY OF VOLATILE ORGANICS PROJECTED TO EXCEED
CRITERIA AT LOW FLOW UNDER CURRENT CONDITIONS
INDIRECT DISCHARGERS (Subcategory A, B, and C)

Pollutant	Average Effluent Pollutant Concentration[a] (µg/ℓ)	POTW Treatment Efficiency	Water Quality Criteria[b] (µg/ℓ) Human Health (W&O)	Water Quality Criteria[b] (µg/ℓ) Aquatic Life (Chronic)	Number of Exceedances Human Health (W&O)	Number of Exceedances Aquatic Life (Chronic)	Known or Suspected Effects
Volatile Organics[c]							
Benzene	971.8	0.98	0.66	265	2(2)	--	C(A)/T
Chloroform	264.1	0.83	0.19	1,240	10(9)	--	$C(B_2)$/M
Chloromethane	2,091.4	0.90	0.19	27,500	15(14)	--	C(NIOSH-X)
1,2-Dichloroethane	760.5	0.88	0.94	20,000	5(5)	--	$C(B_2)$/M
1,1-Dichloroethene	30.6	0.84	0.033	2,400	7(6)	--	C(C)
Methylene chloride	5,925.8	0.95	0.19	9,650	16(15)	--	$C(B_2)$

NOTE:

Total No. of POTWs - 26
Total No. of Facilities - 28
Total No. of Receiving Streams - 25

[a] Concentration discharged from pharmaceutical industry.

[b] For pollutants without EPA criteria, toxic effect levels, reported in the MDSD's Toxics Data Base or estimated using environmental factors, were used.

[c] Criterion for halomethanes has been derived for an entire class of compounds. EPA does not state that each chemical in the class is a carcinogen.

( ) = Number of receiving streams.
C = Carcinogen (CAG designation, if available, or other specified group designation).
M = Mutagen, T = Teratogen
CAG - A = Human carcinogen
B_2 = Probable human carcinogen
C^2 = Possible human carcinogen
NIOSH - x = Potential carcinogen

4. Monitored Impacts of Industrial Discharging Facilities Six of the 25 streams receiving discharges from pharmaceutical facilities discharging to POTWs were monitored for volatile pollutants (Table XII-3). Eight of the 21 evaluated volatile pollutants were detected in water, tissue, or sediments in four of the six stream segments (Tables XII-3 and XII-7). Three of the pollutants exceed human health criteria in three of the six stream segments using a target risk level of 10^{-6} for carcinogens (Tables XII-3 and XII-7). None of the volatile pollutants exceed aquatic life criteria or aquatic life toxic effect levels. In addition, eight of the evaluated pollutants were monitored or limited for 19 percent of the POTWs in PCS (5 of 26) (Tables XII-3 and XII-7).

TABLE XII-7

SUMMARY OF MONITORED POLLUTANT IMPACTS
INDIRECT DISCHARGERS (Subcategory A, B, and C)

Pollutant	Number of Facilities in PCS[a]	Observations in Storet[b] Detected	Not Detected	Known or Suspected Effects[c]
Acrolein			W, S, T	
Acrylonitrile			W, S, T	C(B2)/M/T
Benzene	1	W, S, T		C(A)/T
Bromodichloromethane			W, S, T	C
Chlorobenzene	1		W, S, T	
Chloroethene			W, S, T	C(A)/M
Chloroform	2	W*, S, T		C(B2)/M
Chloromethane			W, S, T	C(NIOSH-X)
1,1-Dichloroethane			W, S, T	
1,2-Dichloroethane	2		W, S, T	C(B2)/M
1,1-Dichloroethene			W, S, T	C(C)
Ethylbenzene			W, S, T	
Methylene Chloride	1	W*, S, T		C(B2)
1,1,2,2-Tetrachloroethane			W, S, T	C(C)
Tetrachloroethene		W*, S	T	C(B2)
Tetrachloromethane			W, S, T	C(B2)/M
Toluene	2	T	W, S	
Tribromomethane			W, S, T	C
1,1,1-Trichloroethane	1	W, S	T	
1,1,2-Trichloroethane		S	W, T	C(C)
Trichloroethene	1	W, S	T	C(B2)/M

NOTE:

[a] Pharmaceutical facilities with monitoring or limits data in the Permit Compliance System (March 1988).

[b] STORET data 1980 to present. Detected = Unremarked or nonzero data. Not Detected = Remarked or zero data. Information is reported for the following sample media: S = Sediment, W = Water, and T = Tissue.

[c] Criterion for halomethanes has been derived for an entire class of compounds. EPA does not state that each chemical in the class is a carcinogen.

* Exceeds human health criteria for ingesting water and organisms (R = 1E-6).

C = Carcinogen (CAG designation, if available, or other specified group designation).
M = Mutagen, T = Teratogen

CAG - A = Human carcinogen
B2 = Probable human carcinogen
C = Possible human carcinogen
NIOSH-X = Potential carcinogen

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XIV. GLOSSARY OF ACRONYMS

AC	Annualized Cost
ACA	Activated Carbon Adsorption
ANPR	Advance Notice of Proposal Rulemaking
BAT	Best Available Technology
BCT	Best Conventional Technology
BMPs	Best Management Practices
BOD	Biochemical Oxygen Demand
BOD_5	Five-Day Biochemical Oxygen Demand
BPT	Best Practical Technology
CC	Capital Costs
CNS	Central Nervous System
COD	Chemical Oxygen Demand
CRF	Capital Recovery Factor
CWA	Clean Water Act
DSE	Domestic Sewage Exclusion
DSS	Domestic Sewage Study
E	Error Term
EOP	End-of-Pipe
EPA	U.S. Environmental Protection Agency
F/M	Food/Microorganism Ratio
GAC	Granular Activated Carbon
GC	Gas Chromatography
HSWA	Hazardous and Solid Waste Amendments of 1984
IFD	Industrial Facilities Discharge
ITD	Industrial Technology Division
LEL	Lower Explosion Limit
MDSD	Monitoring and Data Support Division (EPA)
MEK	Methyl Ethyl Ketone
MF	Monitoring Fee
MGD	Million Gallons Per Day
MLVSS	Mixed Liquor Volatile Suspended Solids
MS	Mass Spectrometry
NPDES	National Pollutant Discharge Elimination System
NRDC	Natural Resources Defense Council
NSPS	New Source Performance Standards
OAQPS	Office of Air Quality Planning and Standards
O&M	Operating and Maintenance Costs
PAC	Powdered Activated Carbon
PCS	Permit Compliance System
PEDCo	PEDCo Environmental, Incorporated
PMA	Pharmaceutical Manufacturers Association
POTWs	Publicly Owned Treatment Works
PSES	Pretreatment Standards for Existing Sources
PSNS	Pretreatment Standards for New Sources
Q	FLowrate
RBC	Rotating Biological Contactor
RCRA	Resource Conservation and Recovery Act of 1976
R&D	Research and Development
RMA	Robert Morris Associates
RSKERL/ADA	Robert S. Kerr Environmental Research Laboratory at Ada, Oklahoma

SCOD	Soluble Chemical Oxygen Demand
SIC	Standard Industrial Classification
SVI	Sludge Volume Index
SVOCs	Semivolatile Organic Compounds
TCLP	Toxicity Characteristic Leaching Procedure
TEPP	Tetraethylpyrophosphate
TOC	Total Organic Carbon
TSS	Total Suspended Solids
TTVOs	Total Toxic Volatile Organics
TVOs	Total Volatile Organics
VFMLS	Viscous Floating Mass of Mixed Liquor Solids
VOCs	Volatile Organic Compounds
WQC	Water Quality Criteria