INTEGRATED MULTIMEDIA
CONTROL ALTERNATIVES

DRAFT Phase I Case Study

NITROSAMINES

Contract 68-01-6020

Gene E. Fax, Project Manager
John Reinhardt, Principal Author

May 18, 1981

Submitted for review to:

Arnold Edelman
Office of Toxics Integration
U.S. Environmental Protection

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SUMMARY OF FINDINGS

Nitrosamines from a large class of compounds many of which are proven carcinogens. These toxic substances have been of great concern to the regulators of different media. Unlike most pollutants, however, nitrosamines are not generally emitted to the environment; rather, they form in various media when their chemical precursors are present. To the extent that nitrosamines have been controlled, most of the present regulations are narrow in scope, dealing with specific media and routes of contamination. For example, FDA regulations limit nitrosamines in malt beverages and EPA regulations limit nitrosamines in certain presticides. The hazardous waste management system regulations include nitrosamines in a general list of toxic constituents, but do not address specific wastes known to contain these chemicals.

Since the regulations have been developed for the most part in response to specific situations, there has not been a systematic multiagency effort to assess the environmental problems associated with nitrosamines. For instance, FDA's recommendation to burn sulfur during the malt drying process cold result in unforeseen air emissions of SO_2. The ad hoc approach is further evidenced by the absence of materials flow analyses. Such an analysis would be very complex because of the problem of formation from precursors in water, air, soil, and animal digestive tracts. The absence of a materials flow analysis prevents estimating overall population exposures to nitrosamines. Further, since there is no estimate of overall population exposure, there can be no accurate assessment of health risks due to exposures from known sources, either individually or collectively.

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3.0 NITROSAMINES

3.1 INTRODUCTION AND FINDINGS

3.1.1 Introduction

The subject of this case study is the degree to which Federal regulatory agencies have taken multimedia effects into account in their rulemaking procedures to control nitrosamines in the environment. Three major issues are the focus of attention:

1. The degree to which each agency, during rulemaking, considered the presence of nitrosamines in media other than the one or ones being regulated at the time.
2. Whether regulatory actions aimed at a particular medium had unanticipated effects on releases of nitrosamines to other media.
3. Whether any gaps in regulatory coverage are apparent.

Other issues are also discussed. These include the extent to which particular regulatory efforts acknowledged similar past or ongoing efforts in other agencies; the technical basis for the standards; and the degree to which economic impacts were included in the decision-making. Findings on these subjects will be incorporated into a cross-substance analysis in a later phase of the project.

There are two issues of particular interest with respect to the regulation of nitrosamines. First, they are mostly formed as a result of chemical reactions in the environment and in food. Second, their presence is a function of the presence of precursors, mainly nitroso compounds and amines. These themes recur in the regulatory histories described in Section 3.2. Substitution of other hazardous products for nitrosamines is not, practically speaking, an important concern, because they usually occur as contaminants, not intentional ingredients. It should be emphasized that the technical interactions illustrated in Exhibit 3.1 are those which are evident from the agency documentation for each action: that is, the preambles to the proposed and final rules, and formal background documents such as Environmental Impact Statements, Criteria Documents, etc. Other interactions between programs - memoranda, meetings, etc.- have not been accessed for this analysis. Therefore, it is likely that more technical interactions took place than are shown. Nevertheless, the formal documentation constitutes the public record of the technical interchange, and this is what the Exhibit reflects.

The outstanding feature of Exhibit 3.1 is the lack of regulatory interactions. Those which took place mostly occurred within EPA. The designation of nitrosamines as toxic pollutants resulted in the promulgation of a Water Quality Criterion and listing by OSW in its disposal and transportation regulations. However, while the hazardous waste disposal regulations usually were influenced by other programs controlling hazardous materials, this was not the case with nitrosamines, which were merely identified. The RCRA regulations do not specifically discuss the disposal of nitrosamines, but mandate that they should be treated as hazardous waste by reason of their toxicity.

FDA and FSQS also have regulatory interactions because of their common regulatory medium, food. FDA has authority to restrict the use of food additives, except for those additives to which USDA had given approval prior to the food additives amendments to the FFCDA. FSQS has authority to classify food as adulterated if it contains deleterious substances.

The scope of the analysis and the sources of information for this study have been described in the introduction to the Lead case study (Section 1.1.1). Also, the general provisions of applicable toxic substance regulations (such as those under RCRA) have already been treated there. In this case study, we examine chiefly those regulatory provisions which deal specifically with nitrosamines.

Nitrosamines were selected for a case study because they exhibit certain interesting characteristics as a pollutants and as regulatory problems. Nitrosamines comprise a large group of substances that are composed of nitroso-compounds and amines. As a group they have a variety of characteristics. They are found in the air, water, soil, food, and the workplace. While nitrosamines are in general highly toxic to animals and humans through acute and chronic exposures, their precursors are less suspect of being directly toxic. Many nitrosamines are considered to be systemic carcinogens; that is, they have been found to induce cancer in certain organs regardless of the route of administration. The environmental ubiquity of nitrosamine precursors , coupled with unknown nitrosamine formation rates, yields a highly uncertain picture of overall exposure. While the seriousness of the health threat posed by nitrosamines demands strict scrutiny and regulatory control, the uncertain magnitude of the exposures denies regulators much of the data needed to delineate and assess the problem. For these reasons, nitrosamines are an interesting subject for a multimedia case study.

3.1.2 Findings: Multimedia Considerations in Rulemaking

Exhibit 3.1 shows the major regulatory actions regarding nitrosamines and the interrelationships among them. Two types of connections are shown: technical interactions (dotted arrows) and intermeshing of regulatory provisions (dashed arrows). The details of these interactions, or rather the lack of interactions, are described in Section 3.2. It is important to note that to the extent past regulatory coordination has taken place among jurisdictions concerned with nitrosamines, it has occurred because of the structures of the relevant acts themselves, not because of initiative among the affected agencies.* Thus, the water programs are statutorily required to give priority to toxic pollutants, and RCRA is intended to regulate wastes generated in part as a result of other regulatory.

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*For the purposes of this report, "regulatory coordination" is defined as occurring when the provision of one rule are specifically designed to complement, supplement, or otherwise take account of the provisions of another rule. Liaison among regulatory agencies occurs constantly; this is not included in the definition of "regulatory coordination" unless the results are visible in the provisions of the regulations.

Turning to the technical interactions among regulatory programs, the Exhibit shows an even more sparse picture. Regulatory programs commonly acknowledged the toxic nature of nitrosamines through the American Conference of Governmental Industrial Hygienists (ACGIH) list of "Industrial Substances suspect of Carcinogenic Potential to Man." OSHA and OWRS both cited the ACGIH, while the FDA and FSQS cited a NIOSH "Hazard Assessment" that was done for OSHA (Reference 1 in Section 3.2.4). However, the impression given by the chart is that there has been little technical interaction across jurisdictions, and hence across media. Section 3.1.2 describes the extent to which intermedia analysis has been included in past and ongoing regulatory efforts.

The attention which regulatory agencies have paid to estimating the flows of nitrosamines into and among the various media has been rudimentary and speculative. The main stumbling block to assessing materials flows of nitrosamines is their characteristic of being contaminants and the products of natural processes, rather than being emitted to the environment directly. This, coupled with the numerous sources of precursors of nitrosamines and their unknown rates of formation, yields too many unknowns to conduct a materials flow analysis. For example, nitroso compounds are found in food, sewage sludge and human saliva. Also, amines are present in air emissions from coking plants and petroleum refinery emissions, in the soil and in the water. These precursors can combine in the environment, in food, or in the human body. Furthermore, formation rates of nitrosamines from precursors can be inhibited by the presence of certain other substances and by pH levels. To further confuse prospective regulators, nitrosamines as a class of substances have a variety of characteristics among themselves. For example, some are volatile while others are not. The complexity of assessing nitrosamines has generally resulted in ad hoc efforts to control a specific form of contamination that has been discovered to pose a health hazard.

The FDA and FSQS regulatory efforts have been mainly concerned with nitrosamine formation resulting from the addition of nitrites to certain foods. The source of nitrosamines was well known to be the addition of the nitrite preservative; therefore, a materials flow analysis would have been inappropriate.

OSHA's regulations do not set standards for nitrosamines in terms of allowable concentrations. Rather, they prescribe methods to minimize worker's exposures. This approach, coupled with the emergency nature of the rulemaking proceedings, gave OSHA little reason or time to study the overall picture of nitrosamines' occurrence in the environment.

Although listed as toxic pollutants, nitrosamines have received little multimedia analysis at EPA's Office of Water Regulations and Standards. The one background document reviewed assessed the probable aquatic fate of three individual nitrosamines. Too little was known about one of the nitrosamines to make a statement about its aquatic fate. The other two were thought to ultimately be destroyed by photolysis. However, the document did not assess the magnitude of the problem of nitrosamines in water.

Most of EPA's regulations treat individual nitrosamines. The regulations do not deal with nitrosamines as a group of substances with a common set of characteristics. However, the Water Quality Criteria Document gave consideration to nitrosamines as a class. This document gave consideration of exposure contributions from other media, but most of the assessment was cursory due to a lack of information. Consequently, the estimates of nitrosamine exposure and accompanying risk factors are based solely on the consumption of water and aquatic organisms. No consideration was given to total exposure risks from other media, such as air, food and the workplace. Documentation for the other two water-related programs, i,e, hazardous spill control and designation of reportable quantities of hazardous spills, did not directly discuss the multimedia effects of including nitrosamines in their programs.

In a report for the Office of Air Quality Planning and Standards (OAQPS), nitrosamine exposure from the air is calculated*. This report does not support any standards specifically regulating nitrosamine levels. However, it is the only attempt at a materials balance approach in the literature. It does not address sources of precursors or multimedia considerations.

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*OAQPS, "Human Exposure to Atmospheric Concentrations of Selected Chemicals: Appendix II - Volume II," May 1980.

3.1.3 Findings: Unanticipated Effects of Regulations

The general lack of quantitative information on intermedia flows of nitrosamines raises the possibility that controlling its emissions in one medium may inadvertently cause its release to another. In this section we examine the extent to which the overall environmental impacts of their actions were foreseen by the rulemakers.

There is a general lack of regulations that specifically limit nitrosamine levels. Consequently, their indirect impacts will be few. However, there are two important unanticipated effects of current regulations. The first arises from the hazardous waste management system order RCRA. The system identifies hazardous waste constituents and then subjects them to a comprehensive "cradle to grave" management system. The onus of identification of hazard constituents is largely with the generator of the waste. None of the RCRA background documents mentioned nitrosamine contaminants in the various industrial waste streams that the OSW analyzed. Therefore, unexpected waste constituents, such as nitrosamines, could escape the management system. The second unanticipated effect is due to FDA's recommended changes in production practices in order to reduce nitrosamine contamination of malt beverages. The FDA recommendation to burn sulfur during the drying of malt could create new contaminants or increase sulfur emissions. Since the FDA recommendation was not an official regulatory action, it did not require the same scrutiny of possible impacts.

3.1.4 Findings: Regulatory Gaps

Detailed analysis of gaps in the control of environmental nitrosamines will be performed in the Phase II report. Nitrosamines present special problems to regulators because they occur as contaminants that may be formed in any medium when their precursors are present. Formation rates can depend on localized conditions, such as pH level. Most of the present regulations address specific known mechanisms of nitrosamine contamination. Consequently, regardless of the medium being regulated, other cases of contamination can be overlooked because of the general lack of data on actual nitrosamine formulation rates. However, in addition to this general problem, certain specific observations have been made in the course of this case study which are described here.

Ambient Air

There are no regulations specifically controlling emissions of nitrosamines into the air. The EPA's OAQPS has estimated that about 215,000 pounds of dimethylamine - a nitrosamine precursor - is emitted in to the air annually, from the actual use of over 71 million pounds of dimethylamine.

Water

Toxic effluent guidelines under the Clean Water Act (Section 307) have not been promulgated for nitrosamines, although it is classified as a toxic substance.

Spills of hazardous substances from industries operating under NPDES permits or from publicly owned treatment works (POTWs) are currently unregulated under the CWA (Section 311). Nitrosamines are classified as hazardous substances.

Soil

POTWs which accept hazardous waste exclusively from small generators are exempt from disposal regulations under Subtitle C of RCRA. Instead, they are allowed to send their sludges to municipal landfills which are approved by states under the provisions of Subtitle D. As noted above, however, approval standards under Subtitle D have not yet been promulgated.

Work place Air

OSHA does not actually limit exposures to DMN, but recommends engineering controls. Unforeseen sources of DMN contamination are unregulated. In addition, mixtures containing 1% of DMN or less are exempt from OSHA's rules. These regulations control DMN only, without regard to the numerous other nitrosamines. OSHA's regulations are based on their assessment that exposures are rare. The number of nitrosamines and the ubiquity of their precursors raise serious doubts concerning OSHA's assessment of the probability of exposure.

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Food

Many of the regulatory actions of FDA and FSQS controlling nitrosamine levels have been implemented through notices of warning. Consequently, formal regulations exist for very few foods such as malt beverages and bacon. These formal regulations were developed in response to specific discoveries of contamination. Presumably other smoked foods, for which FDA has not proposed rules, could also be contaminated.

3.2 Regulatory Histories

3.2.1 Office of Water Regulations and Standards (EPA/OWRS)

3.2.1.1 Toxic Pollutant Effluent Standards

Current Status of Action

Pursuant to Section 307(a)(1) of the Water Pollution Control Act, 33 USC 1317(a)(1), nitrosamines are listed as toxic pollutants (otherwise known as "priority pollutants:" 40 CFR 401.15). As such, they are subject to effluent limitations reflecting "the best available technology ecnomically achievable" (BAT), compliance with which must be attained no later than July 1, 1984 (33 USC s1311(b)(2), 1317 (a)(2)). Furthermore, modification or waiver of the BAT requirements, available for conventional pollutants pursuant to 33 USC s1311(c) and 1311(g), are not allowed for priority pollutants.

EPA policy is to give priority to toxic pollutants in setting industry-based effluent limitations and pretreatment standards. Only one industry's wastewater profiles under these programs have included nitrosamines specifically as a wastewater constituent; that industry was ink formulating. However, nitrosamines were found to be only a contaminant to one plant's wastewater Since there is no evidence in the literature to support the finding of nitrosamines in such wastewater, no further regulatory action was taken.

Section 307(a) of the Clean Water Act authorizes EPA to promulgate effluent standards for toxic pollutants. Section 304(a) authorizes EPA to prescribe "best management practices" to prevent the release of toxic pollutants from "plant site runoff, spillage or leaks, sludge or waste disposal, and drainage from raw material storage." Thus far, no regulations have been promulgated for nitrosamines under either of these sections.

Multimedia Considerations

Since there have been no final roles concerning nitrosamines, it is difficult to assess how the OWRS considers the health hazard presented by nitrosamines in water. The one report described below, discussed information gained from a literature search. The discussions of the three nitrosamines describe their physical chemistry and do not include policy implications.

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The only report issued in support of these actions by the OWRS was released in December of 1979 and was entitled "Water-Related Environmental Fate of 129 Priority Pollutants"(2). This document comprehensively reviews three nitrosamines' persistance and fate as a water pollutants. Seven environmental processes were examined, six of them representing transfers to or within media other than water. The processes were:

Volatilization to air

Photolysis in air

Oxidation in air

Hydrolysis in water

Sorption to sediments

Bioaccumulation in organisms

Biotransformation and biodegradation by organisms

Process rates and residence times in various media were estimated on the basis of secondary sources; the results are shown in Exhibits 3.2, 3.1, and 3.4. While the most probable fate of diphenylnitrosamines in the aquatic environments is presently unknown, the most likely fate of the other two nitrosamines examined is photolytic degradation. The two compounds vulnerable to photolytic degradation also have low volatilization rates. The low volitalization could prevent significant photolysis and consequently these nitrosamines could persist in the aquatic environment.

3.2.1.2 <u>Water Quality Criteria</u>

<u>Current Status of Action</u>

While water quality criteria published by EPA pursuant to Section 304(a)(1) of the Clean Water Act do not have regulatory force, they may be used in setting water-quality-based effluent limitations under Section 302, toxic pollutant effluent standards under Section 307, and state water quality standards under Section 303. These latter standards, in turn, are to be used in establishing individualized effluent limitations for NPDES point source discharge permits under Section 402, as well as best management practices for nonpoint sources under Section 208.

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Water quality criteria for nitrosamines are based on protection of human health and of aquatic life. The EPA has determined nitrosamines to be carcinogens (45 FR 79338). Consequently, the safe level for nitrosamines is zero. Nitrosamine levels protective of human health are calculated parametrically on the basis of various expected levels of incremental cancer risk resulting from ingestion of a) aquatic organisms only and b) aquatic organisms plus water. The derived allowable concentrations are shown in the following table:

Exposure Assumptions (per day)	Risk Levels and Corresponding Criteria ng/l			
	0	10^{-7}	10^{-6}	10^{-5}
2 liters of drinking water and consumption of 6.5 grams fish and shellfish (2)				
N-nitrosodimethylamine	0	0.14	1.4	14.0
N-nitrosodiethylamine	0	0.08	0.8	8.0
N-nitrosodi-n-butylamine	0	0.64	6.4	64
N-nitrosopyrrolidine	0	1.60	16.0	160
N-nitrosodiphenylamine	0	490	4,900	49,000
Consumption of fish and shellfish only.				
N-nitrosodimethylamine	0	1,600	16,000	160,000
N-nitrosodiethylamine	0	124	1,240	12,400
N-nitrosodi-n-butylamine	0	58.7	587	5,868
N-nitrosopyrrolidine	0	9,190	91,900	919,000
N-nitrosodiphenylamine	0	1,610	16,100	161,000

The criteria for acute toxicity to salt water and fresh water aquatic species ranged to 3,300,000 µg/ℓ and 5,850 µg/ℓ respectively. Chronic toxicity was not calculated because of lack of data.

Exhibit 3.2

Summary of Aquatic Fate of Diphenylnitrosamine
(Source: Reference 2, p. 100-4)

Environmental Process[a]	Summary Statement	Rate	Half-Life ($t_{1/2}$)	Confidence of Data
Photolysis	Photolysis may be an important fate process.	-	-	Low
Oxidation	Probably not important	-	-	Low
Hydrolysis	Probably not important.	-	-	Low
Volatilization	Probably not important	-	-	Low
Sorption	No specific data found, may have significance.	-	-	Low
Bioaccumulation	No specific data found, importance difficult to assess.	-	-	Low
Biotransformation/ Biodegradation	Diphenylnitrosamine is both more easily degraded and synthesized than dialkylnitrosamines.	-	-	Low

a There is insufficient information in the reviewed literature to permit assessment of a most probable fate.

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Exhibit 3.3

Summary of Aquatic Fate of Dimethylnitrosamine
(Source: Reference 2, p. 99-5)

Environmental Process	Summary Statement	Rate	Half-Life ($t_{1/2}$)	Confidence of Data
Photolysis[a]	Slow photolysis appears to be the only fate process of any consequence.	–	–	Medium
Oxidation	Probably not important.	-	-	Low
Hydrolysis	Probably not important.	-	-	Low
Volatilization	Probably not important.	-	-	Low
Sorption	Probably not important.	-	-	Low
Bioaccumulation	Probably not important.	-	-	Low
Biotransformation/ Biodegradation	Slow degradation is reported to occur in sewage and soil, but this pollutant appears to be resistant to biodegradation in surface waters.	-	-	Medium

a The predominant environmental process which is thought to determine the fate of the compound.

Exhibit 3.4

Summary of Aquatic Fate of Di-n-prophylnitrosamine
(Source: Reference 2, p. 101-5)

Environmental Process	Summary Statement	Rate	Half-Life ($t_{1/2}$)	Confidence of Data
Photolysis[a]	Slow photolysis appears to be the only fate process of any consequence.	-	-	Medium
Oxidation	Probably not important.	-	-	Low
Hydrolysis	Probably not important.	-	-	Low
Volatilization	Probably not important.	-	-	Low
Sorption	Probably not important.	-	-	Low
Bioaccumulation	Probably not important.	-	-	Low
Biotransformation/ Biodegradation	Slow degradation is reported to occur in sewage and soil, but this pollutant appears to be resistant to biodegradation in surface waters.	-	-	Medium

a. The predominant environmental process which is thought to determine the fate of the compound.

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Multimedia Considerations in the Regulatory History

The developmental history of the present water quality criteria for toxic pollutants was reviewed in detail in the Lead case study (Section 1.2.3.3). In this discussion, we shall deal only with those actions specific to nitrosamines.

The first mention of nitrosamines in the water quality criteria program was in the Federal Register notice of 15 March 1979 (44 FR 15926) asking for comments on proposed criteria for 27 of the 65 toxic pollutants. The introduction to the proposed criteria made clear that in the case of confirmed or suspected carcinogens, EPA would assume that there is no scientific basis for estimating "safe" levels. Instead, the agency would give a range of concentrations estimated to pose alternate degrees of incremental cancer risk ranging from 10^{-7} to 10^{-5}. These concentrations were to be presented for informational purposes, and were not to be interpreted as being "safe," the only known safe level being zero. The risk estimates were to be extrapolated from animal experiments to humans using the conservative "one-hit" model endorsed by the IRLG agencies.

The 15 March notice provided discussions of individual pollutants which were summaries of the respective Draft Water Quality Criteria Documents. While the salt water and fresh water aquatic toxicology of nitrosamines were still being researched, nitrosamines' carcinogenicity had been well established in the literature. The Federal Register on November 28, 1980 announced the availability of the final versions of the water quality criteria documents for several pollutants, including nitrosamines (45 FR 79318). The level of nitrosamines calculated to present the various levels of risk of cancer to humans as extrapolated from animals studies were generally lower in the final criteria than in the proposed criteria. Since the EPA did not note any methodological change, the differences must have been due to inclusion of new data from new animal toxicology studies.

The Water Quality Criteria Document (3) for nitrosamines was divided into aquatic and mammalian toxicology. The document reviewed the routes of exposure (see Exhibit 3.5) and discussed the relative importance of each route's contribution. The risks of exposure were calculated based on a person's probable consumption of water and/or aquatic organisms. While other routes of exposure were discussed, they were not incorporated because of inadequate data. An attempt to quantify total exposure was deemed inappropriate by the EPA because exposures would have had to include nitrosamines and their precursers. The problem of estimating precursors and their rate of formation into nitrosamines is confounded by the impact of a variety of environmental factors, such as temperature, pH, and the presence of other substances. To further confuse the undertaking of such a risk assessment, the chapter on pharmacokinetics concluded that the metabolic pathways of nitrosamines were indeterminable at the present time.

In reviewing the literature, the water quality criteria document found that nitrosamines were acutely toxic to every animal species tested, poisonous to humans, powerfully mutagenic, teratogenic, and possibly carcinogenic. Nitrosamines were found to induce cancer in small multiple dosages and in the EPA's "one dose" method when administered orally. While other routes of exposure, such as inhalation, were not proven to induce cancer, nitrosamines were regarded as systemic carcinogens, i.e., able to induce cancer in a number of body sites regardless of the route of exposure. The document presented a brief description of the contributions of various media, including through food, air and occupation. However, the lack of information on the of extent nitrosamine contamination, because of the numerous unknown factors in nitrosamine formation, prevented a fully comprehensive risk assessment.

3.2.1.3 Designation of Hazardous Substances and Reportable Quantities

Current Status of Action

Nitrosamines (specifically diethylnitrosamine and dimethylnitrosamine) have been proposed as hazardous substances pursuant to Section 311(b)(2)(A) of the Clean Water Act (45 FR 46094). No final action has been taken. Under 40 CFR Part 117, reportable quantities have been established for all hazardous substances identified in 40 CFR Part 116. Any discharge into navigable waters of the United States or adjoining shorelines of a hazardous substance that is equal to or in excess of its

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Exhibit 3.5

Calculated Daily Human Exposure to N-nitroso Compounds **
(Source: Reference 3, p. c-15)

	Daily intake (μg)			
	Nitrosodimethylamine + Nitrosodiethylamine	Nitrosopyrrolidine	Nitrosonornicotine	Other
Nitrite preserved foods, 100 g.	1	5		
Tobacco smoke, 20 cigarettes	2		3	
Drinking water, New Orleans				8*
Air, factory site	40			10*
Herbicide formulation, 1 ml spill	640			

*Tentative, unconfirmed identification as N-nitroso compound.
**Source: Fine, et al. 1977a

reportable quantity must be immediately brought to the attention of the Coast Guard (40 CFR 117.21), and the discharger is subject to cleanup liability and civil penalities (40 CFR 117.22-23).

Certain types of discharges are excluded from regulation under 40 CFR parts 116 and 117, including those in compliance with permits issued under the Marine Protection, Research and Sanctuaries Act; the Federal Insecticide, Fungicide and Rodenticide Act; the Resource Conservation and Recovery Act; and the dredge and fill provisions and NPDES provisions of the Clean Water Act. Under certain circumstances, discharges from a point source in violation of its NPDES permit are also exempt.

Multimedia Considerations in the Regulatory History

The general history of how hazardous substances were designated has been described in the Lead case study (Section 1.2.2.4), and will not be repeated here. It is useful to recall in discussion of nitrosamines, however, that while the hazardous substance determination was originally based on aquatic toxicity, EPA announced in February of 1979 the intent to expand the criteria to include carcinogenicity, mutogenicity, teratogenicity, bioaccumulation, and other long-term effects (44 FR 10270).

Nitrosamines were not on the initial list of hazardous substances which was promulgated on 13 March 1978 (43 FR 10474). The proposal to include nitrosamines on that list was made on 9 July, 1980 (45 FR 46094). The reason for including nitrosamines was based on their suspected carcinogenicity to humans.

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References for Section 3.2.1

1. U.S. Environmental Protection Agency, Effluent Guidelines Division, "Development Document for Proposed Effluent Limitations Guidelines, New Source Performance Standards and Pretreatment Standards for the Ink Formulating Point Source Category," December, 1979, EPA-440/1-79/090-6.

2. Callahan, M.A., et. al., "Water Related Environmental Fate of 129 Priority Pollutants," 2 volumes, December, 1979, Report EPA - 440/4-79-0299a.

3. U.S. Environmental Protection Agency, "Ambient Water Quality Criteria for Nitrosamines," October, 1980, EPA 440/5-80-064.

3.2.2 Office of Solid Waste (EPA/OSW)

3.2.2.1 Hazardous Waste Management System (EPA/OSW)

A full discussion of the hazardous waste management system authorized by the Resource Conservation and Recover Act (RCRA) has been presented in the Lead case study (Section 1.2.5). It includes a description of the following components 1) identification and listing mechanism for hazardous wastes, 2) standards for generators, 3) standards for transporters, and 4) standards for owners and operators of treatment, storage, and disposal facilities for hazardous waste.

Hazardous wastes containing nitrosamines are subject to regulation under RCRA's Hazardous Waste Management System via three identification and listing routes. The first is through nitrosamines' listing in 40 CFR 261 (Appendix VIII) as a toxic waste constituent. Another is through nitrosamines' inclusion as one of the 65 toxic pollutants under the CWA, Section 307. Lastly, nitrosamine is also specifically listed for regulations pertaining to discarded commercial chemical products, off-specification species, containers, and spill residues thereof (40 CFR 261.33).

Multimedia Considerations

Congress intended the hazardous waste management system under RCRA to have a very broad scope. Consequently, regulations under RCRA are process oriented rather than pollutant-oriented because of the wide variety of hazardous waste stream constituents in existence. In order to create a comprehensive list of hazardous waste constituents, the OSW analyzed a number of industrial waste streams. This analysis not only served to identify the variety of currently used disposal practices, but to enumerate waste constituents. The voluminous background document (1) that reviewed the various industrial processes did not identify nitrosamines in any of the industries included in the report. The environmental impact statement for Subtitle C of RCRA (2) also reviews certain industrial waste streams. The EIS identifies nitrosamines in the following two industrial waste streams: 1) miscellaneous acyclic chemicals and chemical products industry and 2) the "red water" wastestream from the explosives industry. The "red water" waste stream was specifically included in the regulations as a specific source of hazardous wastes (40 CFR Part 261.32). While the other industry was not specifically included in the identification portion of the RCRA regulations. The "red water" waste stream was classified by the EPA as a reactive waste, not a toxic waste. Since nitrosamines are toxic and not reactive, nitrosamines were probably not considered in EPA's analysis of disposal methods and potential health risks.

Nitrosamines are listed in the regulations under RCRA as a toxic waste constituent (40 CFR Part 261.11). These constituents have been shown by scientific studies to be toxic, carcinogenic, mutagenic, or teratogenic to humans or other forms of life (45 FR 33121). Wastes with toxic waste constituents would be classified as hazardous unless the administrator specifically determines through specified criteria that the waste was not capable of posing a health hazard to humans (45 FR 33121). While the hazardous waste management system regulations indicated a strong effort to coordinate efforts within EPA and with other agencies, no mention of other regulatory efforts concerning nitrosamines were specifically mentioned.

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References for Section 3.2.2

1. Environmental Protection Agency, "Subtitle C-Background Document for Identification and Listing of Hazardous Wastes 40 CFR Part 261.31 and 261.32," April, 1980.

2. Environmental Protection Agency, "Draft-Final Environmental Impact Statement - Part 1: Subtitle C, Resource Conservation and Recovery Act of 1976," April 1980.

3. Environmental Protection Agency, Carcinogen Assessment Group, "Risk Assessment on Trifluralin," October 18, 1978.

3.2.3. Office of Pesticide Programs (OPP)

3.2.3.1 Registration of Pesticides

Current Status of Actions

The Office of Pesticide Programs (OPP) has published a Notice of Rebuttable Presumption against Registration (RPAR) for the pesticide trifluralin, which contains greater than 1 part per million of the nitrosamine N-nitroso-di-n-propylamine (NDPA) (44 FR 50911). The registration process is fully discussed in the Lead Case Study (Section 1.2.6). The other action taken by OPP on nitroso-contaminated pesticides was a notice of proposed policy in June of 1980 (45 FR 42854). The proposed policy requires manufacturers of nitroso-contaminated pesticides to submit information on nitrosamine level and composition. This information will be used to eliminate pesticides that do not have sufficient nitrosamine contamination to warrant the costly RPAR process. The lack of information concerning nitroso-contamination was stated as the reason for delay of their regulation.

Multimedia Considerations in the Regulatory History

On October 28, 1976, the EPA stopped registration of new pesticides that were probably contaminated with nitroso-compounds (45 FR 42855). A preamble to a later regulation notice stated that this action was initiated because nitrosamines were generally toxic and frequently carcinogenic. Since that moratorium on registration, the OPP has analyzed 300 compounds and has found three main routes of contamination (45 FR 42855).

- during manufacturing processes
- during storage with corrosive inhibitors
- contamination of ingredients, e.g., dimethylamines in amine reagents

In 1977, the OPP first required nitroso-containing pesticide manufacturers to submit analytical data concerning nitrosamine contamination of their products (42 FR 51640). The information requested concerned instances of nitrosamine contamination of products during the manufacturing process. The Notice also mentioned the presence of nitrosamines in pesticide containers as anti-corrosive agents.

On 30 August, 1979, the OPP took its first action to limit nitrosamine contamination of pesticides (44 FR 50911). The action established an RPAR on the basis of NDPA's oncogenic risk (40 CFR Part 162.11(a)(3)[ii]). NDPA's orcogenic effects were stated as a matter of fact, without references. The RPAR refused to grant registration to trifluralin with greater than 1 ppm of NDPA. The position document appearing with the RPAR stated that the OPP used information from the Department of Agriculture and other sources to develop its risk assessment of trifluralin use (45 FR 50914). Populations at risk included agricultural workers, nursery workers, and the population at large. No specific exposure rates were stated in the document. The economic consequences of the cancellation of the use of trifluralin were also calculated. OPP calculated that the 5 years following cancellation would produce a $300 million dollar loss in farm income; but the benefits of lower exposure levels of nitrosamines were not discussed. It was noted that the nation's sole producer of trifluralin currently produced the pesticide with less than 1 ppm of NDPA. The risk assessments done by the EPA's Carcinogen Assessment Group (CAG) in 1977 and 1978 had assumed a much higher level of NDPA contamination (1 and 2). The CAG study done in 1978, at OPP's request, analyzed the risk of trifluralin use In addition to reviewing the medical studies' findings that NDPA contaminant was oncogenic, the study calculated exposure risks to the general population and to herbicide applicators (see Exhibits 3.6 and 3.7). The risk to the general population eating contaminated food was calculated assuming an NDPA level of 5 ppm in the trifluralin. The conservative estimates concluded a very low risk to the population at large. These estimates were outdated at the time of the RPAR because of reductions in NDPA levels achieved in the interim by the sole producer of trifluralia.

In June of 1980, the OPP requested more information to achieve regulation of nitroso-contaminated pesticides within a reasonable time. This information will be used to eliminate pesticides that do not have sufficient nitrosamine contamination to warrant the costly RPAR process. The OPP stated that the reduction of the number of pesticides requiring revieww was necesary because subjecting over 900 pesticides to the RPAR process was impractical.

Exhibit 3.6

Estimate of Cancer Risk to the General Population from Ingestion of NDPA Associated with the Use of Treflar (Trifluralin) on Food Crops

(reference ; see pg. 36)

Food Type	Trifluralin Tolerance, t_1 (mg/kg of diet)	Fraction of Food in Diet, a_1	Maximum Daily NDPA Intake, X_1 ($\times 10^{-9}$) (mg/kg of diet)[1]	Lifetime Individual Risks ($\times 10^{-9}$)[1]	Total Number of Cases in Lifetime[2]
Asparagus	.05	.0014	.35	.14	.0308
Carrots	.95	.0048	22.8	9.12	2.01
Citrus Fruits	.05	.0381	9.53	3.81	.838
Corn, grain	.05	.01	2.5	1.0	.22
Cottonseed	.05	.0015	.375	.15	.033
Curcurbits	.05	.0284	7.1	2.84	.625
Fruiting Veg.	.05	.0299	7.48	2.99	.546
Grapes/Raisins	.05	.0049	1.23	.49	.108
Hops	.05	.0003	.075	.03	.0066
Leafy Veg.	.05	.0276	6.9	2.76	.607
Mung beans	2.0	.0003	3.0	1.2	.264
Nuts	.05	.001	.25	.10	.022
Peanuts	.05	.0036	.90	.36	.0792
Peppermint	2.0	.0003	3.0	1.2	.264
Root Crop Veg.	.05	.11	27.5	11.0	2.42
Safflower	.05	.0003	.075	.03	.0066
Seed/pod Veg.	.05	.0366	9.15	3.66	.805
Spearmint	2.0	.0003	3.0	1.2	.264
Stone Fruits	.05	.0125	3.13	1.25	.275
Sugar, cane and beet	.05	.0364	9.1	3.64	.801
Sunflower	.05	.0003	.075	.03	.0066
Wheat	.05	.1036	25.9	10.4	2.28
All Foods			143.4	57.4	12.6

[1] Column entries are multiplied by the factor in the column heading, i.e. for asparagus the daily intake is 0.35×10^{-9} mg/kg/day and the individual risk is 0.14×10^{-9}.

[2] Assuming 2.2×10^{8} people are exposed to food.

Risk Estimates for Treflar (Trifluralin) Applicators

(reference (2); see pg. 34)

Crop	Number of People	Inhalation Exposure, I (ug/year)	Dermal Exposure, D (ug/year)	Lifetime Individual Risk ($\times 10^{-7}$)[1]	Lifetime Number of Cases ($\times 10^{-3}$)
Soybeans	156,491	0.12	1.33	1.3	21.0
Cotton	55,576	0.11	1.08	1.1	6.2
Tomatoes	13,490	0.04	0.42	.43	.58
Cole Crops	4,162	0.04	0.50	.49	.20
Beans	23,689	0.07	0.75	.76	1.8
Tree and Vine	3,985	0.07	0.75	.76	.30
Hops	51	0.23	2.74	2.7	.014
Potatoes	1,800	0.05	0.50	.52	.093
Carrots	647	0.07	0.83	.82	.053
Okra	856	0.02	0.17	.19	.016
Greens	3,259	0.01	0.17	.15	.050
Spanish Peanuts	4,474	0.06	0.59	.61	.27
Celery	166	0.11	1.33	1.3	.022
Peppers	2,267	0.02	0.17	.19	.042
Mint	55	0.18	2.16	2.1	.012
Dill	16	0.08	0.91	.91	.0014
Alfalfa	320	0.07	0.83	.82	.026
Spring Wheat	890	0.34	4.07	4.0	.36
Mustard Seed	68	0.12	1.33	1.3	.0091
Safflower	933	0.27	3.24	3.2	.30
Sunflower	5,523	0.13	1.50	1.5	.82
Sugar Beets	5,178	0.14	1.66	1.6	.84
Sugar Cane	116	0.40	4.65	4.6	.053
Cucumbers	3,030	0.01	0.17	.15	.046
Cantaloupes	335	0.03	0.33	.33	.011
Watermelon	2,718	0.02	0.25	.24	.066
Dry Peas	202	0.13	1.41	1.4	.029
English Peas	2,776	0.04	0.42	.43	.12
Field Peas	156	0.04	0.42	.43	.0067
Commercial Applicators (all crops)	3,800	0.14	1.74	1.7	.64
Totals	297,029				34.0

[1] Column entries are multiplied by the factor in the column heading; i.e. for cotton the risk is 1.1 and the number of cases os 6.2×10^{-3}.

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References for Section 3.2.3

1. U.S. Environmental Protection Agency, Carcinogen Assessment Group, "Carcinogenic Risks of Contamination of the Herbicides Treflar, Trysber and Benzae," May 10, 1977.

2. U.S. Environmental Protection Agency, Carcinogen Assessment Group, "Risk Assessment on Trifluralin," October 18, 1978 (Revised December 20, 1978).

3.2.4 Occupational Safety and Health Administration (OSHA)

3.2.4.1 Occupational Exposure to Dimethylnitrosamine (DMN)*

Current Status of Action

No permissible exposure limit is stated for DMN; instead, the current OSHA regulation (29 CFR 1910.1016) specifies engineering controls for workplaces where the chemical is handled. Manufacturing, processing, storing or other handling must take place in a "regulated area;" access to such an area is restricted to workers wearing protective clothing. DMN handling or processing must be done in closed systems or with adequate ventilation; ventilation exhaust air must be "decontaminated" before it can be released to the general environment. However, specific methods for decontamination, and maximum DMN concentrations in the treated exhaust air, are not specified.

Processing and handling of mixtures containing less than 1% DMN by weight or volume are exempt from OSHA regulations.

Multimedia Considerations in the Regulatory History

Immediately after the passage of the Occupational Safety and Health Act of 1970, the Administrator of OSHA used his powers under Section 6(a) to promulgate as mandatory standards the Threshold Limit Values (TLV's) adopted by the American Conference of Governmental Industrial Hygienists.** These TLV's, and hence the resulting OSHA standard, did not include tolerances for nine substances, including DMN, which the ACGIH had identified as human or animal carcinogens. As a result, OSHA was in the position of having acknowledged these substances as workplace carcinogens without having required any corresponding remedial measures. To correct this discrepancy, OSHA requested assistance from the National Institute of Occupational Safety and Health (NIOSH) in developing occupational health standards for carcinogens. In response, NIOSH published a list of fifteen substances (taken from the 1972 ACGIH TLV document, plus alpha-napthylamine) with a request for any information which could be helpful in writing Criteria Documents for these materials (37 FR 13285).

*The OSHA designation for the chemical name of DMN is N-Nitrosodimethylamine.

**ACGIH, Threshold Limit Values of Airborne Contaminants in Workroom Air, 1971.

The regulation of DMN, among the other carcinogens listed by NIOSH, was accelerated in December of 1972 when the Oil, Chemical and Atomic Workers' Union (OCAW) submitted to OSHA a petition which proposed an emergency standard for 10 alleged carcinogens. The proposed standard specified that "no exposure or contact by any route, respiratory, oral, or skin shall be permitted for any of the following substances or other substances containing them." DMN was one of the listed substances. The proposal went on to specify housekeeping, personal protection, environmental monitoring, medical examinations, recordkeeping, and labelling procedures. The OCAW proposal also provided that the Assistant Secretary of Labor should promulgate additional regulations specifying safe methods of disposal for carcinogen-contaminated materials and carcinogens (including DMN), after consulting with the Administrator of EPA.

In response to the OCAW petition and subsequent public comments on it, OSHA issued an Emergency Temporary Standard (ETS) on 3 May 1973 (38 FR 10929). Rejecting the union's "no-exposure" approach, the ETS specified a system of restricted-access handling areas, protective clothing, change rooms, and other work practices to minimize employee contact with DMN and the other carcinogens. Mixtures containing less than1% by weight of any carcinogen were exempted from the standard. The brief preamble to the ETS contained no statements bearing on technical or policy issues surrounding the standards' provisions.

The promulgation of the Emergency Temporary Standard for carcinogens resulted automatically in the initiation of rulemaking proceedings for a permanent standard, under the provisions of Section 6(c) of the Occupational Safety and Health Act. Accordingly, a permanent standard identical to the ETS was proposed by OSHA in July of 1973 (38 FR 18900). The brief preamble contained no technical discussion, but referred to the Draft Environmental Impact Statement, issued at the same time, in support of the proposal. This Draft EIS is not now available; however, on the basis of the Final EIS (reviewed below) we may conclude that it dealt with no media other than workplace air, and even in that case it did not discuss concentrations or the extent of employee exposure.

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In preparation for the final rule, OSHA and NIOSH produced several background studies. In July of 1973, NIOSH published a "Hazard Review of N-Nitrosodimethylamine" (1), which reviewed the experimental evidence for DMN's carcinogenicity. It concluded that the substance had been demonstrated to produce cancers at many sites, by a variety of administration routes, and in many animals, including mice, hamsters, guinea pigs, rabbits, and several species of fish. No discussion of DMN in the workplace or the general environment was provided. The second report, issued by OSHA in August of 1973, was entitled, "Some Economic Aspects of an Occupational Safety and Health Standard for the Use of Fourteen Carcinogenic Compounds" (2). The report contained two- to three-page writeups on each of the fourteen carcinogens, describing the chemicals themselves, their origins, uses, users, and the costs of complying with the proposed rule. No analysis was contained in the report; most of its content was based on statements made by manufacturers and users themselves. Nevertheless, the descriptions contained OSHA's first official statement of the scope of the problem. In the case of DMN, the agency was solely concerned with its use in research laboratories. This use was reported by four firms and one university, and a total of 23 employees were judged to be potentially exposed. The document acknowledged that DMN had been used as an industrial solvent, in the synthesis of rocket fuel, and for several other end uses. However, it concluded that the use of the chemical in these capacities must have ceased, since "none of the respondents to the standard reported any of these uses." Total production for 1972 was estimated at "less than 6 kilograms." No account was taken of DMN as a contaminant of other workplace chemicals (e.g., cutting oils), or as a breakdown product in foods.

OSHA's 1973 portrayal of DMN as a rare substance exposing only a few laboratory workers to risk is dramatically contradicted by recent EPA data showing that in 1978 approximately 71.8 million lb/yr was produced; that the chemical was being used in many chemical manufacturing processes; and that about 215,000 lb/yr was being emitted to the atmosphere.* OSHA's

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*Science Applications Inc., "Human Exposure to Atmospheric Concentrations of Selected Contaminants", 1981.

oversight can likely be ascribed to the fact that the backup data for the Fourteen Carcinogens standard was assembled in only three months, and the agency was forced to rely almost exclusively on submissions by users and manufacturers.

The third document prepared in support of the rule was the "Final Environmental Impact Statement: Proposed Regulation--Handling of Certain Carcinogens" (3). The technical content of the Final EIS was derived almost entirely from the two reports mentioned earlier. OHSA did include a discussion of the relation between the proposed rule and other federal actions, but none of the actions mentioned related to DMN. The EIS did not mention any environmental media other than the workplace.

The final carcinogens rule was promulgated on 29 January, 1974 (39 FR 3756); its provisions have already been summarized above. Besides reiterating the toxicological evidence reported in the NIOSH Hazard Survey, the preamble clarified several points which arose in OSHA's development of the rule. One issue was the relevance of animal tests to standards designed to protect humans; OSHA's position was that substances proven carcinogenic in animals, but not in humans, should be treated as if they were known hazards to people. This policy was chosen because it was "responsible and correct;" no scientific support was offered. The zero-tolerance standard proposed by the OCAW petition was rejected, because

> ". . . no possible exposure to the carcinogens under any circumstances could only be guaranteed by a total ban on the manufacture, use (even for cancer research), and transportation of the substances . . . Accordingly, the intent of the standards is to reduce exposure of workers to any of the listed substances to the maximum extent possible consistent with continued use."

Finally, exclusions of liquids or mixtures containing less than a specified percentage of the controlled substances was justified in order

> "to avoid substantial obstruction, if not stoppage, of the use of many processes and products which are considered useful in industry and even in cancer research, and about which the record contains very little information."

Exempted concentrations were set at 1% for the eight substances (including DMN) designated as animal carcinogens, and 0.1% for the six substances considered to be human carcinogens. The inconsistency with the earlier argument, that the two categories should be treated equally, was not noted.

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References for Section 3.2.4

1. National Institute for Occupational Safety and Health, Office of Research and Standards Development; "Hazard Review of N-Nitrosodimethylamine (DMN)," July, 1973.

2. Occupational Safety and Health Administration, Office of Standards; "Some Economic Aspects of an Occupational Safety and Health Standards for the Use of Fourteen Carcinogenic Compounds," undated (pose-August 10, 1973).

3. ______________, Final Environmental Impact Statement: Proposed Regulation--Handling of Certain Carcinogens," September 28, 1973.

3.2.5 Food and Drug Administration (FDA)

3.2.5.1 Nitrosamines (DMN and NDELA)

Current Status of Actions

On April 10, 1979 the FDA issued a notice requesting the cosmetic industry to reformulate a variety of products in order to reduce the probability of nitrosamine formation (44 FR 21365). The notice requested removal of aklarolamine-containing ingredients that may act as nitrosating agents to form N-nitrosodietharolamine (NDELA). Thus far, the FDA is satisfied with the industry's response and no further regulatory action is being considered.

Pursuant to Section 406 of the Federal Food, Drug and Cosmetic Act, the FDA set an action level for dimethylnitrosamines (DMN) in malt beverages at 5 parts per billion (45 FR 39341). The FDA, in the June 10, 1980 Federal Register notice, stated that it will take regulatory action upon discovery of an excess of the DMN action level for malt beverages.

Multimedia Considerations in the Regulatory History

The only action the FDA has taken to control nitrosamines in cosmetics has been a Federal Register Notice warning industry of the problem on April 10, 1979.

The industry warning on NDELA contamination in cosmetics was based on 1) toxicological studies of NDELA and 2) recent studies showing percutaneous absorption of NDELA. While aklarolamine-containing ingredients were cited as the main nitrosating agent to be removed, its substitutes and their impacts were not discussed. Since this notice was merely a recommendation to industry, and not an exercise of specific regulatory authority, no documentation of the notice's impact was generated.

The FDA regulated another nitrosamine, this time in malt beverages, by publishing an "action level" in the Federal Register on June 10, 1980. While the FDA had established the action level in a press release of October 29, 1979, it incorporated the "administrative guideline" into its regulations officially in June of 1980. As an adminsitrative guideline, the action level did not require a public comment period.

The action level for DMN in malt beverages was based on the lowest level that DMN can be reliably measured, not because 5 ppb is considered safe. The justification for the action level is provided in an "action guide" that accompanied the notice (45 FR 39341). The FDA stated in the policy guide that since DMN is a carcinogen, that there was no safe dosage. The FDA concluded that a safe dosage for a carcinogen had not been determined to date.

The carcinogenicity of DMN was formally documented in 1973 in a review of its hazard potential.[1] This document reviews the experiments conducted that tried to assess DMN's acute and chronic toxicity. The review concludes that because of DMN's potency in inducing cancer in a variety of sites, administration methods and animals, that DMN is a potential human carcinogen. To accomplish the reduction of levels of DMN in malt beverages, the FDA recommended the burning of sulfur during the drying of the barley, since the kiln-drying of malt was identified as the primary path of contamination. The FDA did not discuss possible adverse impacts of burning sulfur such as newly created air emissions or the formation of other hazardous substances in combination with the sulfur or contaminants thereof.

3.2.5.2 Nitrites/Nitrates

Current Status of Actions

The FDA has proposed a rule giving nitrites and nitrates food additive status in poultry products under the Federal Food, Drug and Cosmetic Act (44 FR 75662). This action proposes that no prior regulation authority exists for this use of nitrites and nitrates in poultry products by the Food Safety and Quality Service (FSQS). The FSQS, under the Federal Meat Inspection Act, that predates the Food Additive Amendments to the Federal Food, Drug and Cosmetic Act of 1958, has approved the use of nitrites to certain meat and meat products as preservatives. The FSQS approval is considered a preemption of FDA's jurisdiction by providing approval to nitrites used as preservatives in meats before they had been scrutinized by FDA's Food additive approval process. The FDA is contending in the proposed regulations for nitrites in poultry, that no such prior approval, i.e., prior sanction, exists.

The use of nitrites in bacon was considered for regulation under the color additive provisions of the Act. However FDA's final action withdrew nitrites from consideration as a color additive because it was determined that they do not impart color.

Nitrites in meat and fish were regulated in about 1960 by the FDA. The following standards are found in 21 CFR 172.160-172.177:

Potassium nitrate in cod roe . . . . 200 ppm

Potassium nitrate in sable fish, salmon, shad, and meat. 500 ppm

Sodium nitrite in tuna . . . . 10 ppm

Sodium nitrite in chub . . . . 100-200 ppm

Sodium nitrite in sable fish, salmon and shad. . . . . 200 ppm

The FDA has no recent final rules regulating nitrite levels in food.

Multimedia Considerations in the Regulatory History

Nitrites are included in this case study of nitrosamines because they are precursors of nitrosamines. The formation of nitrosamines through the combination of nitrites and amines (a class of substances that are ubiquitous in the environment) occurs in the environment, in food processing, theoretically during digestion, and possibly in the process of inhalation. Nitrates are also included, because their tendency to be transformed into nitrites.

Since the FSQS and the FDA have regulatory authority of the levels of nitrites in foods, the two agencies have closely coordinated regulatory efforts. On August 15, 1980, the two agencies published a report questioning the recent finding that nitrites themselves were carcinogenic (2). A 1978 study at the Massachusetts Institute of Technology (MIT)* was responsible for the regulatory community's consideration of nitrite's carcinogenicity. The jointly published report concluded that the MIT study was not sufficient to suspect nitrites of being carcinogens. The

*Dr. Newberne, "Final Report to FDA for Contract FDA 74-2181, August, 1978.

FDA has published its own assessment of the MIT study which concurred that the matter required more investigation (3). If nitrites themselves had been shown to be cardinogenic, then the FDA would have been required to ban its use by mandate of the Delaney Clause to the FFDCA (to be discussed below). Consequently nitrites are regulated solely on the basis of their being precursers of nitrosamines. However, the carcinogenicity of nitrosamines is thoroughly referenced throughout the preambles of the FDA's regulations.

The fact that nitrites produce nitrosamines in food is delaying the setting of final permissible nitrite levels. The delay is due to the interpretation of the Delaney Amendment to the Federal Food, Drug and Cosmetic Act of 1962. Originally, this amendment was interpreted to disallow any presence of carcinogens in food. However, due to advances in measurement techniques, the discovery of ever smaller amounts of contaminants has forced the FDA to reinterpret the Delaney Amendment through the establishment of a "constituent policy" (see Exhibit 1). The constituent policy when it is proposed, will state the methodology for developing dosages of carcinogens that will present an acceptable risk level to exposed populations (44 FR 17070). This policy, to be proposed in the Federal Register around June, 1981, will heavily influence the final resolution of permissible nitrite levels.

Regulation and control of nitrosamine levels in foods is not as simple as the FDA setting limits on allowable levels of nitrosamines because of the problem of precursors. Nitrites and amines, precursors of nitrosamine formation, combine in several media and under a variety of circumstances. The contamination of foods with nitrosamines through a variety of exposure routes has required the FDA to formulate the constituent policy. The constituent policy will enable the FDA to determine at what minimum level that the nitrosamine contaminant will be considered too small to have a significant impact. The FDA will use this policy to regulate a number of carcinogens including nitrosamines. The

FDA's need for the constituent policy has precluded any quantification of the magnitude of various routes of nitrosamine contamination. Since the FDA does not have jurisdiction over the routes of contamination, there was very little consideration of regulations.

Coordination between FDA and FSQS was caused by the question of prior regulatory authority of nitrites by the FSQS. No multimedia issues needed to be resolved, merely a definition of which agency had the legal authority to regulate nitrite levels in various foods.

3.2.6 Food Safety and Quality Service (Department of Agriculture/FSQS)

3.2.6.1 Entry Into Official Establishments, Reinspection and Preparation of Products

Current Status of Action

The Food Safety and Quality Service (FSQS) of the DOA has promulgated only one final rule that limits nitrosamines directly. This rule requires that nitrosamines in bacon be lower than the lowest confirmable level, i.e., 5 parts per billion (ppb) (43 FR 20992). However, the FSQS also regulates the levels of nitrites and nitrates because they are precursors to nitrosamine formation in certain foods. In general, the FSQS must get approval for food additive usage from the FDA as mandated by the Federal Food, Drug and Cosmetic Act. Nitrites and nitrates, however, are exempt from the need for FDA approval because their use as preservatives predates the amendments that require FDA approval of food additives. Use of nitrates in bacon has been banned since May 16, 1978 (43 FR 20992). Nitrites serve as a preservative and inhibit the formation of clostridium botulinum. Since nitrites serve such important functions, they were not banned but limited in bacon to 120 ppb (43 FR 20992). In addition, the regulations required that if nitrites are added to bacon, then prescribed amounts of sodium ascorbate or sodium erythorbate must also be added. Sodium ascorbate and sodium erythorbate prevent the combination of nitrites and amines into nitrosamines. Also on May 16, 1980, the FSQS proposed rules to further reduce nitrite use to 40 ppm (43 FR 21007), but no final action has taken place. Final action will occur pending the substantiation of the prevention of botulism at 40 ppm of nitrites.

The other final ruling by FSQS in February, 1979, authorizes the use of acid-producing microorganisms in the processing of bacon to inhibit nitrosamine formation (44 FR 9372).

The FSQS proposed a ban on nitrite use in baby, junior and toddler meat products in April, 1978 (43 FR 18193). While no final action has been taken on this ban, the preamble to the proposed ban noted that industry had voluntarily taken nitrites out of baby, junior and toddler foods.

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Multimedia Considerations in the Regulatory History

DOA first limited nitrite use in 1925, restricting residual nitrite levels in products to 200 parts per million. The proposed reduction of nitrites in November of 1975 was based on the recommendations by a multiagency study group, including the FDA, HEW and USDA (40 FR 52614). Since there was some controversy about whether or not the regulation of nitrites was under the authority of the USDA the FDA has been consulted frequently on this issue. A panel of experts of agencies and private industry, cited in the preamble above, published a report of recommendations and minutes of their meetings. In Final Report on Nitrites and Nitrosamines: Report to the Secretary of Agriculture (1), the panel recommended the measures which were subsequently promulgated. The discussions centered on the carcinogenicity of nitrites, mitigating agents that could be added, the process of the formation of nitrosamines, and the value of nitrites in curbing botulism. The carcinogenicity of nitrosamines themselves was considered to be well established and was consequently not discussed in detail in the report.

The other document generated in support of DOA's actions on nitrites was "An Analysis of A Ban on Nitrite Use in Curing Bacon" (2). This analysis reviewed current regulation and speculated on the impact of a ban of the use of nitrites in bacon. It did not compare economic and health benefits because of the complexities of quantifying increased health due to unknown reductions in cancer rates. Most of the report dealt with the economic impact of such a ban. The study described two scenarios with different substitution assumptions for nitrite-preserved bacon. It concluded that farm income would drop 2.5 percent over the first 5 years of the ban. No mention of multimedia considerations were included in the report.

The final rule allowing acid-producing micro-organisms in meat products to mitigate nitrosamine production by lowering the pH was accomplished as an emergency measure on February 13, 1979 (44 FR 9372). The emergency measure is authorized by Executive Order 12044 and Secretary of

Agriculture's Memorandum of 1955. Consequently no proposed rule was issued. An Impact Analysis statement was noted in the preamble, but was unavailable for review and inclusion in this report.

At present, the FSQS is still monitoring and studying the problem. The agency's consideration of nitrosamines in a multimedia perspective is limited by its narrow statutory authority.

References for Section 3.2.6

1. United States Department of Agriculture, "Final Report on Nitrite and Nitrosamines: Report to the Secretary of Agriculture," February, 1978.

2. United States Department of Agriculture, Ecoomics, Statistics and Cooperatives Service, "An Analysis of a Ban on Nitrite Use in Curing Bacon," March, 1979.

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APPENDIX

Federal Register Notices Reviewed for Nitrosamines Case Study

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CHEMICAL: Nitrosamines

AGENCY: EPA

STATUTE: Water Pollution Control Act, 33 USC s1251 et. seq.

PROGRAM: Effluent limitations; Section 301(b), 33 USC s1311(b), 40 CFR Parts 402-699

FR/DATE	CFR	ACTION	DESCRIPTION
40 FR 8302 2/26/75	40 CFR Part 447	Proposed Rule	Proposed BPT and BAT effluent limitations for Ink Formulating Point Source Category
40 FR 31724 7/28/75	40 CFR Part 447	Final Rule	Final BPT and BAT effluent limitations for Ink Formulating Point Source Category; zero discharge of process wastewater pollutants required
45 FR 928 1/3/80	40 CFR Part 447	Proposed Rule	Proposed BPT and BAT effluent limitations for revised Ink Formulating Point Source Category; zero discharge of process wastewater pollutants required (nitrosodiphenylamine found in wastewater).

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CHEMICAL: Nitrosamines

AGENCY: EPA

STATUTE: Water Pollution Control Act, 33 USC s1251 et. Seq.

PROGRAM: New Source Performance Standards, Section 306, 33 USC s1316
40 CFR Parts 402-699

FR/DATE	CFR	ACTION	DESCRIPTION
40 FR 8302 2/26/75	40 CFR Part 447	Proposed Rule	Proposed NSPS for Ink Formulating Point Source Category; zero discharge of process wastewater pollutants required
40 FR 31724 7/28/75	40 CFR Part 447	Final Rule	Final NSPS for Ink Formulating Point Source Category; zero discharge of process wastewater pollutants required
45 FR 928 1/3/80	40 CFR Part 447	Proposed Rule	Proposed NSPS for revised Ink Formulating Point Source Category; zero discharge of process wastewater pollutants required (nitrosodiphenylamine found in wastewater)

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CHEMICAL: Nitrosamines

AGENCY: EPA

STATUTE: Water Pollution Control Act, 33 USC s1251 et. Seq.

PROGRAM: Pretreatment Standards - Existing Sources; Section 307(b), 33 USC s1317(b); 40 CFR Parts 402-699

FR/DATE	CFR	ACTION	DESCRIPTION
40 FR 31730 7/28/75	40 CFR Part 447	Proposed Rule	Proposed PSES for Ink Formulating Point Source Category; zero discharge of pollutants into POTWs required
45 FR 928 1/3/80	40 CFR Part 447	Proposed Rule	Proposed PSES for Ink Formulating Point Source Category; zero discharge of pollutants into POTWs required (nitrosodiphenylamine found in wastewater)

DRAFT

CHEMICAL: Nitrosamines

AGENCY: EPA

STATUTE: Water Pollution Control Act, 33 USC s1251 et. Seq.

PROGRAM: Pretreatment Standards - New Sources; Section 307(c), 33 USC s1317(c); 40 CFR Parts 402-699

FR/DATE	CFR	ACTION	DESCRIPTION
40 FR 8302 2/26/75	40 CFR Part 447	Proposed Rule	Proposed PSNS for Ink Formulating Point Source Category; zero discharge of wastewater pollutants required
40 FR 31724 7/28/75	40 CFR Part 447	Final Rule	Final PSNS for revised Ink Formulating Point Source Category; zero discharge of process wastewater pollutants required
45 FR 928 1/3/80	40 CFR Part 447	Proposed Rule	Proposed PSNS for revised Ink Formulating Point Source Category; zero discharge of process wastewater pollutants required (nitrosodiphenylamine found in wastewater)

DRAFT

CHEMICAL: Nitrosamines

AGENCY: EPA

STATUTE: Water Pollution Control Act, 33 USC s1251 et. Seq.

PROGRAM: Water Quality Standards and Criteria; Sections 303, 304(a), 33 USC 1313, 1314(a); 40 CFR Parts 120

FR/DATE	CFR	ACTION	DESCRIPTION
44 FR 15926 3/15/79		Notice	Notice of availability for public comment of water quality criteria for 27 of the 65 toxic pollutants, including nitrosamine standards for fresh and salt water aquatic life and and human health
45 FR 79318 11/28/80		Notice	Notice of availability of water quality criteria documents, including nitrosamine standards for fresh and salt water aquatic life and human health

DRAFT

CHEMICAL: Nitrosamines

AGENCY: EPA

STATUTE: Water Pollution Control Act, 33 USC s1251 et. Seq.

PROGRAM: Toxic Pollutant Effluent Standards; s307(a)(1), 33 USC s1317(a)(1); 40 CFR Parts 129, 401

FR/DATE	CFR	ACTION	DESCRIPTION
43 FR 4109 1/31/78		Notice	List of toxic pollutants, including nitrosamines, published pursuant to s307 (a)(1)
44 FR 44501 7/30/79	40 CFR s401.15	Final Rule	List of toxic pollutants, including nitrosamines, relisted at 40 CFR s401.15

DRAFT

CHEMICAL: Nitrosamines

AGENCY: EPA

STATUTE: Water Pollution Control Act, 33 USC s1251 et. Seq.

PROGRAM: Designation of Hazardous Substances and Reportable Quantities; s311(b)(2)(A), 33 USC s1321(b)(2)(A); 40 CFR Parts 116, 117

FR/DATE	CFR	ACTION	DESCRIPTION
44 FR 10270 2/16/79	40 CFR Part 116	Advance Notice of Proposed Rulemaking	Notice that EPA is considering the expansion of selection criteria for hazardous substances to include chronic and long-term effects, including carcinogenicity
45 FR 46094 7/9/80	40 CFR Part 116	Proposed Rule	Proposed addition to hazardous substance list of 14 carcinogens, including DMN and diethylnitosamine
45 FR 46097 7/9/80	40 CFR Part 117	Proposed Rule	Proposed reportable quantities for DMN (1 lb.) and diethylnitrosamine (1 lb.)

DRAFT

CHEMICAL: Nitrosamines

AGENCY: EPA

STATUTE: Resource Conservation and Recovery Act, 42 USC s. 6901 et. seq.

PROGRAM: Hazardous Waste Management System, Sections 1006, 2002 (a), 3001-7, 3010, 7004; 42 USC ss.6905, 6912(a), 6924-25; 40 CFR Parts 260-65

FR/DATE	CFR	ACTION	DESCRIPTION
45 FR 33119 5/19/80	40 CFR Part 261	Interim Final Rule	Listing of hazardous wastes; Nitrosamines listed as hazardous waste constituent (40 CFR Part 261, App. VIII)
45 FR 74884 11/12/80	40 CFR Part 261	Final Rule	Final listing of hazardous constituents (40 CFR Part 261, App. VIII)
45 FR 78532 11/25/80	40 CFR Part 261	Final Rule	Final listing of hazardous wastes and toxic wastes (40 CFR ss.261.33[e] and [f]
46 FR 11127 2/5/81	40 CFR Part 264	Proposed Rule	Proposed standards for hazardous waste facilities, including prohibition on discharging nitrosamines into present or future drinking water sources (40 CFR s.264.20 [b])

DRAFT

CHEMICAL: Nitrosamines

AGENCY: EPA

STATUTE: Federal Insecticide, Fungicide and Rodenticide Act (FIFRA), (as amended by the Federal Environmental Pesticide Control Act (FEPCA)), 7 USC 136 et. seq.

PROGRAM: Pesticide Registration, 40 CFR Parts 162, 165, 180

FR/DATE	CFR	ACTION	DESCRIPTION
42 FR 51640 9/29/77		Notice	In anticipation of EPA policy statement on pesticides containing N-nitroso contaminants, applicants and registrants of these products are required to submit data
44 FR 50911 8/30/79	40 CFR Part 162	Notice	Statement of policy; issuing an RPAR for Trifluralin and restricting NDPA levels to <1ppm
45 FR 42854 6/25/80		Notice	Statement of policy re N-nitroso contaminants in pesticides, establishing new data requirements, proposing risk criteria for registration/RPAR process, describing methods for reducing risk and establishing regulatory priorities

DRAFT

CHEMICAL: Nitrosamines

AGENCY: FDA

STATUTE: Federal Food, Drug and Cosmetic Act, 21 USC s.201 et. seq.

FR/DATE	CFR	ACTION	DESCRIPTION
42 FR 44376 9/22/77		Notice	Notice of FDA determination that nitrites and Nitrates used in poultry products are food additives, outlining conditions under which they can continue to be used and establishing of issues concerning their safety
44 FR 21365 4/10/79		Notice	Notice that FDA has detected nitrosamines in certain topically applied cosmetics; manufacturers requested to take steps to eliminate them while FDA continues to study the problem
44 FR 75659 12/21/79	21 CFR Part 70	Proposed Rule	Proposed ruling that nitrites in bacon and other meat products qualify for exception to the color additive definition of the FFDCA and hence are not to be regulated under the act
44 FR 75662 12/21/79	21 CFR Part 170	Proposed Rule	Proposed ruling that use of nitrites and nitrites and nitrates in poultry products does not have prior sanction and hence can be regulated as a food additive

DRAFT

CHEMICAL: Nitrosamines

AGENCY: FDA

STATUTE: Federal Food, Drug and Cosmetic Act, 21 USC s.201 et. seq.

FR/DATE	CFR	ACTION	DESCRIPTION
45 FR 39341 6/10/80	21 CFR 109.6	Notice	Notice of availability of FDC Compliance Policy Guide setting regulatory action level for DMN in beer at 5 ppb.
45 FR 77043 11/21/80	21 CFR Part 70	Withdrawal of Proposed Rule	FDA decision that nitrites in bacon are not color additives under FFDCA; proposed rule of 12/21/79 withdrawn because there is no longer any need to decide whether nitrites in bacom qualify for exception to color additive provisions

DRAFT

CHEMICAL: Nitrosamines

AGENCY: FSQS (also Animal and Plant Health Inspection Service)

STATUTE: Federal Meat Inspection Act, 21 USC 601 et. seq.
Poultry Products Inspection Act, 21 USC 451 et. seq.

PROGRAM:

FR/DATE	CFR	ACTION	DESCRIPTION
40 FR 52614 11/11/75	9 CFR Parts 318, 381	Proposed Rule*	Limits nitrites and nitrates used in meat and poultry products; limits residual nitrite to 200 pmm; bans nitrite use in infant and junior food; limits nitrites in bacon to 125 ppm with ascorbate or erythorbate added.
42 FR 55626 10/18/77		Notice	Request for data from industry on whether use of nitrates and/or nitrites in meat products results in formation of carcinogenic nitrosamines
43 FR 18193 4/28/78	9 CFR Part 318	Proposed Rule	Proposed ban on use of nitrites and nitrates in baby, junior and toddler meat products; proposed regulation allowing use of same name on products containing reduced levels of nitrites and nitrates
43 FR 20992 5/16/78	9 CFR Part 318	Final Rule	Final regulations prohibiting use of nitrates in bacon, requiring the use of 125 ppm of nitrites and 550 ppm of sodium or sodium eythorbate; creating a monitoring program for nitrosamines levels; also requires maximum of 10 ppb nitro samines in bacon and 5 ppb within one year of the ruling

* By Animal and Plant Health Inspector Service before FSQS was formed.

DRAFT

CHEMICAL: Nitrosamines (continued)

AGENCY: FSQS (also Animal and Plant Health Inspection Service) (continued)

STATUTE: Federal Meat Inspection Act, 21 USC 601 et. seq.
Poultry Products Inspection Act, 21 USC 451 et. seq.

PROGRAM:

FR/DATE	CFR	ACTION	DESCRIPTION
43 FR 21007 5/16/78	9 CFR Part 318	Proposed Rule	Proposed reduction 44 ppm - Na 49 ppm - K and potasium sorbate of the amount of nitrites required to be used in bacon
43 FR 39120 9/1/78	9 CFR Part 38	Proposed Rule Revision	Includes a requirement to include 550 ppm of sodium ascorbate or sodium erytharbate with nitrite reduction to block nitrosamine formation in 43 FR 21007
44 FR 9372	9 CFR	Final Rule (No proposed rule, because under emergency)	Final rule authorizing; the use of acid producing micro-organisms in the processing of bacon for the purpose of inhibiting information of nitrosamines
45 FR 43425 6/27/80	9 CFR Part 318	Proposed Rule	Proposed rule extending monitoring program to dry-cured bacon and required use of certain preservative techniques
45 FR 43447 6/27/80		Notice	Report of FSQS on its continuing study of the use of nitrites and nitrates in cured meat products

DRAFT

CHEMICAL: Nitrosamines

AGENCY: OSHA

STATUTE: Occupational Safety and Health Act of 1970, 29 USCs ss.651-78

PROGRAM: Occupational Safety and Health Standards, Sections 6 and 8, 29 USC ss.655 and 657; 29 CFR Parts 1910, 1927 and 1990

FR/DATE	CFR	ACTION	DESCRIPTION
37 FR 13285 7/6/72		Notice	Request for data on 15 inspected carcinogens, including DMN; notice of intent to develop workplace standards for these substances
38 FR 4037 2/9/73		Notice	Notice of receipt of petition for issuance of emergency temporary workplace standards for 10 inspected carcinogems, including DMN
38 FR 10929 5/3/73	29 CFR Part 1910	Notice	Emergency temporary standard prescribing workplace standards and procedures for 14 carcinogens, including DMN
38 FR 18900 7/16/73	29 CFR Parts 1910, 1927	Proposed Rule	Proposed adoption of above temporarily standards as permanent workplace standards and procedures for 14 carcinogens, including DMN (Part 1910); Proposed permit program for employers using any of the carcinogens identified in Part 1910 (Part 1927)

DRAFT

CHEMICAL: Nitrosamines

AGENCY: OSHA

STATUTE: Occupational Safety and Health Act of 1970, 29 USCs ss.651-78

PROGRAM: Occupational Safety and Health Standards, Sections 6 and 8, 29 USC ss.655 and 657; 29 CFR Parts 1910, 1927 and 1990

FR/DATE	CFR	ACTION	DESCRIPTION
38 FR 20074 7/27/73	29 CFR Part 1910	Final Rule	Revision of emergency temporary standards adopted at 38 FR 10929
39 FR 3756 1/29/74	29 CFR Part 1910	Final Rule	Final workplace standards and procedures for 14 carcinogens, including DMN (29 CFR s.1910 .93p)
12/17/74	29 CFR Part 1910		3rd Cir Ct of App vacates laboratory provisions for all 14 carcinogens, including DMN
40 FR 23072 5/28/75	29 CFR s1910.1016	Notice	DMN regulation (29 CFR s1910.93p) renumbered 29 CFR s1910.1016

DRAFT

CHEMICAL: Nitrosamines

AGENCY: OSHA

STATUTE: Occupational Safety and Health Act of 1970, 29 USCs ss.651-78

PROGRAM: Occupational Safety and Health Standards, Sections 6 and 8, 29 USC ss.655 and 657; 29 CFR Parts 1910, 1927 and 1990

FR/DATE	CFR	ACTION	DESCRIPTION
42 FR 54148 10/4/77	29 CFR Part 1990	Proposed Rule	Proposed general rule concerning the identification and regulation of toxic substances in workplace that may pose carcinogeic risk
45 FR 5002 1/22/80	29 CFR Part 1990	Final Rule	Final general rule concerning the identification, classifidation and regula- of toxic substances in workplace that pose carcinogrenic risk
45 FR 53672 8/12/80		Notice	List of substances that may be reviewed for possible regulation as carcinogens, including Diphenylamine 4 nitroso, and Diphenylamine-N-nitroso

DRAFT

CHEMICAL: Nitrosamines

AGENCY: CPSC

STATUTE: Consumer Product Safety Act, 15 USC s 2051 et. seq.

PROGRAM: Chronic Chemical Hazards Program

FR/DATE	CFR	ACTION	DESCRIPTION
45 FR 61344 9/16/80		Notice	Request for public comment on list of 91 chemicals that CPSC has preliminarily determined are not present in products under its jursidiction, including DMN and other nitrosamines

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