The Information Content of Premanufacture Notices

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Preface

Some chemicals have been associated with deleterious effects on human health and the environment. Responding to concerns that newly developed chemicals might pose risks to health or the environment, Congress included provisions in the Toxic Substances Control Act that require manufacturers and importers of new chemicals to notify the Environmental Protection Agency (EPA) before new chemicals are introduced into commerce. The implementation of those provisions began in July 1979, and the EPA has now received more than 1,500 Premanufacture Notices that describe new chemicals.

The Office of Technology Assessment (OTA) prepared this background paper, "Information Content of Premanufacture Notices," in response to a request from the Subcommittee on Commerce, Transportation, and Tourism of the House Committee on Energy and Commerce. OTA examined 740 Premanufacture Notices, and this study reports the results of analyzing those notices for the presence or absence of the information specified by the Toxic Substances Control Act and for other items of physical-chemical and toxicity information that are useful for estimating potential health and environmental effects. In addition, this study reports the regulatory and voluntary compliance actions that EPA has taken as a result of reviewing Premanufacture Notices.

The general finding of this study is that the amount of information contained in Premanufacture Notices varied widely. Every notice contained most or all of the information items specified in the law, and many also reported nonspecified and useful information about the characteristics and toxicity of the chemical. At the same time, about half of the notices did not contain any toxicity data. This absence is not surprising given that the law does not require companies submitting Premanufacture Notices to carry out toxicity studies, but only to notify EPA of toxicity data that they have available.

Certainly, the absence of toxicity data complicates EPA's efforts to decide whether a new chemical may present an unreasonable risk to health or the environment. But the importance of toxicity data for making decisions about particular chemicals varies. Those data are less important for chemicals that closely resemble others for which there is much information and experience. They are critical for unusual chemicals or chemicals for which there is limited information. An additional study would be necessary to evaluate the EPA's decisionmaking process and whether or not it was compromised by absent data. The last chapter of this report outlines such a study.

OTA background papers are prepared by OTA staff and contractors, and drafts of the papers are sent for review to interested organizations and individuals. This paper was written by Michael Gough and Stedman Stevens; John Bell designed computer formats and programs. The 30 individual and organizational reviewers of the first draft are listed in appendix C.

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Contents

Chapter *Page*

I. Summary 3

2. "New Chemicals" and the Toxic Substances Control Act. 11
Regulation of New Chemicals 11
Actions Available to EPA Following PMN Reviews 12
Public Notice of New Chemicals Considered for Manufacture 14
PMN Reporting Requirements 14
EPA Management of PMN Review 15
Proposed Exemptions to the PMN Reporting Requirements 16
Risk Assessment 19
Structural Activity Relationship Analysis and Its Use in PMN Review 20

3. Methods Used in Study of Information Content of Premanufacture Notices. 25
PMNs Examined by OTA 25
Inspection of PMN Files 26
Information Collected From PMNs 27
Security Precautions To Protect Confidential Business Information 29
EPA Cooperation 29
Analysis of the Data... 30
Organization of the Presentation of the Analysis . 30

4. Frequency of Submission of TSCA-Specified Data on Premanufacture Notices 33
Numbers of PMNs Submitted to EPA 33
Chemical Name and Production Volumes. ....,.. 34
Chemical Formulae and Structures 35
Byproducts 36
Uses 37
Number of Workers Exposed and Disposal 37
Summary of Findings About Reporting of TSCA-Specified Information 38

5. Frequency of Submission of Physical-Chemical Information on Premanufacture Notices ..,.... 41
How Many Physical-Chemical Data Were Submitted on PMNs? 41
Physical-Chemical Data Were Reported More Frequently unmanufactured PMNs 43
Submission of Physical-Chemical Data on PMNs of Different Classes 44
Summary of Findings About Submission of Physical-Chemical Data 45

6. Frequency of Submission of Toxicity Information on Premanufacture Notices 49
How Many Toxicologic Data Were Submitted on Pans? 50
Toxicity Data Were Reported More Frequently on Manufactured PMNs 52
Submission of Toxicity Data on PMNs Describing Different Classes of Chemicals 53

Page

7. Submission of Physical-Chemical and Toxicity Information on Some Subgroups of Premanufacture Notices 57
PMNs Submitted for Consumer Products 57
PMNs Submitted for Polymers 58
PMNs Submitted for Site-Limited Chemicals 59
PMNs Submitted for Low-Production-Volume Chemicals 60
Comparison of Toxicity Data Submitted on Consumer and Nonconsumer Substances, Both Polymers and Nonpolymers, Scheduled for Production indifferent Amounts 62
Magnitude of Scale-Up in Production of Low-Volume Chemicals 64
Are PMNs Submitted for Imported Chemicals More Complete Than Those Submitted for Other Chemicals?. 66

8. Actions Taken by the Environmental Protection Agency as a Result of Reviewing Premanufacture Notices 69

9. Discussion 75
Frequency of Reporting of Information on Premanufacture Notices 75
Data Submitted on PMNs That Described Chemicals Intended for Consumer Use 75
Data Submitted on PMNs That Described Chemicals Proposed for Exemption From PMN Review 76
Usefulness of Submitted Information for EPA's Risk Assessment Process 77
Possible Further Evaluation of the PMN Review Process 78

Appendix A: Summary of Topics Considered at Evaluation Meeting During Initial Screen of Premanufacture Notices at the Environmental Protection Agency 83

Appendix B: Copies of Face Sheets: EPA and CMA PMN Forms 84

Appendix C: Acknowledgments 86

Appendix D: Acronyms and Glossary 88

References 90

Tables

Table No. *Page*

1. Proposed Low-Volume and Site-Limited Intermediate Exemption Provisions 17
2. Proposed Polymer Exemption Provisions 17
3. Completeness of PMNs for TSCA-Specified Information 35

Contents—Continued

Table No. *Page*

4. Number of Class 1, 2, and 3 PMNs That Have Name, Structure, and Formula 35
5. Number of PMNs Describing Chemicals Intended for Industrial, Commercial, and Consumer Uses 37
6. Items of Physical-Chemical Information That Were Scored on PMNs. 41
7. Number of Physical-Chemical Data Items Submitted on PMNs. 42
8. Completeness of PMNs for Physical-Chemical Information as a Function of the Time Between End of the Review Period and the Commencement of Manufacture 44
9. Physical-chemical Information on PMNs Describing Class 1, Class 2, and Class 3 Chemicals 44
10. Items of Toxicity Information That Were Scored on PMNs. 49
11. Eight General Classes of Short-Term Tests That Measure Mutagenicity or Other Interactions With DNA 50
12. Number of Toxicologic Items Submitted on PMNS 50
13. Completeness of PMNs for Toxicity Information as a Function of the Time Between End of the Review Period and the Commencement of Manufacture 52
14. Toxicity Information on PMNs Describing Class l, Class 2, and Class 3 Chemicals 53
15. Completeness of PMNs Submitted for Consumer-Use Products as Compared to Other PMNs. 57
16. Physical-Chemical and Toxicity Information Submitted for Site-Limited Chemical PMNs and All Other PMNs 59
17. Physical-chemical and Toxicity Information Submitted on PMNs That Project Initial Year Production Volumes of 1,000 Kilograms or Less, of Between 1,001 and l0,000 Kilograms, and All Others 61
18. Number of Submissions of Toxicity Data on Polymers and Nonpolymers To Be Produced indifferent Amounts 63
19. Number of Submissions of Toxicity Data on PMNs Describing Consumer-Use Chemicals and Polymers and Nonpolymers To Be Produced in Different Amounts 63
20. Number of Submissions of Toxicity Data on PMNs Describing Nonconsumer-Use Chemicals and Polymers and Nonpolymers To Be Produced in Different Amounts 64

Table No. *Page*

21. Estimated First Year Production Volumes, and Increases Expected in the Third Year. 65
22. Physical-Chemical and Toxicity Information Submitted for Import PMNs and All Other PMNS 66
23. EPA Summary of Informal Regulatory Actions in Fiscal Years 1979, 1980, 1981, and First Three Quarters of Fiscal Year 1982 70
24. Estimated Costs of Tests That Might Be Reported on PMNs 78

Figures

Figure No. *Page*

1. Letter of Request for This Background Paper 4
2. Disposition of PMNs Submitted From July 1979 and Including All Those That Completed the 90-Day Review Period by the End of September 1981 25
3. Form Used by OTA in Collection of Data From PMNs 28
4. Number of Valid PMNs Received Each Month: April 1979 Through June 1982 34
5. Percentage of PMNs Containing the Three Most Commonly Reported Toxicity Tests and the Two Tests Related to Chronic Toxicity and Ecotoxicity . . . . , ... 51
6. Percentage of Polymer and Nonpolymer PMNs That Contained the Three Most Commonly Reported Toxicity Tests and Tests Related to Chronic Toxicity and Ecotoxicity. 54
7. Percentage of PMNs That Described Consumer-Use or Nonconsumer-Use Products and Contained the Three Most Commonly Reported Toxicity Tests and Tests Related to Chronic Toxicity and Ecotoxicity 58
8. Percentage of PMNs That Describe Site-Limited or Other Chemicals and Contained the Three Most Commonly Reported Toxicity Tests and Tests Related to Chronic Toxicity and Ecotoxicity . 60
9. Percentage of PMNs That Described Low-or High-Production-Volume Chemicals and Contained the Three Most Commonly Reported Toxicity Tests and Tests Related to Chronic Toxicity and Ecotoxicity 62

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Summary

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Summary

The Premanufacture Notice (PMN) Program is the U.S. Government's effort to identify toxic substances before they enter commerce, to impose controls when necessary, and thereby to reduce unreasonable risks to human health and the environment. The Toxic Substances Control Act (TSCA) requires that a Premanufacture Notice be submitted to the Environmental Protection Agency (EPA or the Agency) at least 90 days before a new chemical is manufactured or imported into the United States.

Using the information in the PMN and professional judgment, EPA reviews each PMN to determine if the chemical described in the notice presents or may present an unreasonable risk to human health or the environment. When EPA does not conclude that an unreasonable risk may be associated with the substance described in a PMN, manufacture of the chemical can begin at the end of the 90-day PMN review period.

In the event that EPA determines that the substance presents or will present an unreasonable risk, the Agency can regulate its manufacture.

If EPA decides that the information presented in the PMN is: 1) insufficient for the Agency to make a reasoned evaluation of the health and environmental effects that might be associated with the substance, and 2) that the substance may either (a) present an unreasonable risk or (b) be produced in quantities such that there will be substantial environmental or human exposure, the Agency can restrict or ban the manufacture of the substance pending the submission of additional appropriate data.

When exposure to the substance under the conditions of use described in the PMN is of no concern to EPA, but the Agency has concerns about potential risks under other conditions of use, the Agency can write an order requiring submission of more data before the substance can be manufactured for a "significant new use."

A PMN is to contain certain information about the new chemical to enable EPA to make decisions necessary to protect human health and the environment under the provisions of TSCA. Because TSCA does not allow EPA to require that information be generated about a substance simply because the substance is new, it was expected that the amount and type of information present on PMNs would vary.

The PMN program differs significantly from a premarket testing program that was adopted by the European Economic Community (EEC) and was considered for adoption by the Organization for Economic Community and Development (OECD) (3). The PMN program requires the submission of data within the possession of the submitting company, and TSCA forbids EPA from ordering the generation of test data simply because the chemical described on the PMN is new. In practice, this means that data the company generates in its normal course of business are submitted to EPA.

The EEC program requires the submission of specified test data, whether or not the submitting company would have generated those data in its normal course of business. In other words, the EEC approach requires testing. Furthermore, as production volumes increase, EEC requires the submission of additional data. In contrast, once a new chemical has completed PMN review, it is no longer subject to regulation as a new chemical. Both the PMN and the EEC programs may add exemptions and make other alterations to their general requirements. The General Accounting Office is now preparing a report that compares the OECD system to the PMN program; the report is expected to be completed in late 1983.

This OTA background paper responds to a request for a report that describes the nature and extent of information reported on PMNs in general and on PMNs submitted for certain subgroups of chemicals, such as those that have now entered manufacture, and on EPA's use of those data in decisionmaking about new chemicals (fig. 1). It reports the examination of all PMNs received by EPA in the first 2 years of the program's opera-

Figure 1.—Letter of Request for This Background Paper

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U.S. House of Representatives
Subcommittee on Commerce, Transportation, and Tourism
of the
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WASHINGTON, D.C. 20519

June 7, 1982

Dr. John H. Gibbons
Office of Technology Assessment
600 Pennsylvania Avenue, S.E.
Washington, D. C. 20510

Dear Dr. Gibbons:

As you are aware, there has been considerable debate in recent months regarding the effectiveness of the premanufacturing notice (PMN) provisions of the Toxic Substances Control Act (TSCA). Concerns regarding the impact of these provisions on innovation have been addressed in numerous studies including the OTA'S just completed assessment, "Technological Innovation and Health, Safety, and Environmental Regulations". However, little, if any, assessment has taken place regarding (1) the extent to which current PMN submissions either fulfill or compromise efforts to perform the preventive health **and environmental protection mandate of the Act, and (2) the expected** effects of EPA's proposed exemptions from the PMN process.

Questions in this regard surfaced repeatedly during the Subcommittee's reauthorization hearings on TSCA, though few objective answers could be rendered due to the scarcity of independent assessment of these questions. Given the substantial nature of these outstanding concerns, and in light of the OTA's assessment, "Technologies for Determining Cancer **Risks from the Environment", which encom**passes both toxic substances risk assessment and regulatory analysis, the Subcommittee is requesting that OTA review TSCA's PMN provisions and submissions. The assessment should include the following components:

(1) Characterization of the notices received to date regarding classes of chemicals and their uses.

(2) Assessment of data that were submitted on (a) different classes of chemicals, (b) substances that were subsequently placed on the market as compared to those that were not, and (c) substances that would be exempted from PMNs under EPA's currently proposed changes;

Figure 1.—Letter of Request for This Background Paper—Continued

June 7, 1982
Page 2

(3) Analysis of the impact of the original data submissions on subsequent EPA decisions under the PMN section.

The Subcommittee anticipates that the OTA would use the recommendations of the Organization for Economic Cooperation and Development (OECD) and other appropriate organizations on premanufacturing testing policy in its assessment of the new chemical testing program under TSCA. In addition, it is expected that the OTA would observe all rules and procedures regarding the protection of confidential data used in the assessment.

Sincerely,

James J. Florio, Chairman
Subcommittee on
Commerce, Transportation and Tourism

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tion (through June 1981) and those submitted in June 1982. In addition, the data reported on PMNs that describe chemicals of certain specified classes were analyzed separately. For instance, PMNs that describe chemicals that, according to EPA records, are now being manufactured were arialyzed and compared to those that described chemicals that have not yet been manufactured.

EPA is considering exempting some classes of chemicals from PMN reporting requirements. PMNs submitted for the classes of chemicals likely to be exempted—chemicals used and consumed only at the site of manufacture, chemicals to be manufactured in amounts of less than 10,000kilograms annually, and polymers-were also analyzed separately.

To collect the information reported in this background paper, 45 items for which data might be submitted on PMNs were identified. The presence or absence of each of the 45 items was recorded and the frequency of submission of the items for all PMNs and some subsets of PMNs was computed.

TSCA, by mandating the submission of available data, leaves to the submitting company decisions about which data are to be developed. Therefore, the reported data reflect company decisions about what data are important. The absence of data from PMNs makes EPA's task of deciding whether anew chemical may bean unreasonable risk more difficult. On the other hand, the fact that a submitting company does not have to submit data that it regards as unnecessary represents a saving to the company, and if the chemical presents no risk, then both society andthe company benefit.

If EPA decides that particular data are necessary for the evaluation of a new chemical and that such

data are absent from the PMN, the Agency can make an informal request for the data, or it can write an order requiring their submission. Whichever mechanism is used to ask for the data, the burden is on EPA to show that the data are necessary. Requiring submission of more data, especially toxicity data, would reduce the number of times that EPA makes decisions without such data. It would also place the burden for developing data on the submitting companies.

In some cases, the absence of important information—of types that neither the company nor EPA recognizes as essential-may compromise the protection that the Agency affords to human health and the environment. Requiring the submission of a list of test results would guard against that happening, but at the same time, some of the required data might be unnecessary-at least for some chemicals. In those cases, the costs of developing that information would not reduce risks to human health or the environment.

In general, the frequency with which PMNs contained the TSCA-specified and required information items about the identity of the chemical, its expected production volumes, its likely uses, the number of workers who might be exposed in their places of employment, and methods for its disposal was high. More than 90 percent of all PMNs reported those items. One TSCA-specified reporting requirement, that the PMN identify byproducts associated with the manufacture or processing of the chemical, was less frequently met. Only 67 percent of PMNs reported byproduct information. Overall, 62 percent of PMNs reported all TSCA-specified information; 86 percent reported all but byproduct information.

Additional physical and chemical information beyond that which is specified in TSCA was reported on 96 percent of all PMNs, and at least one item about toxicity was reported on 53 percent. OTA looked at physical-chemical and toxicity information reported on some subgroups of PMNs, and found more frequent reporting on PMNs that describe substances that are more likely to be hazards. For instance, reporting of both physical-chemical information and toxicity data was more frequent on PMNs that described substances which, according to EPA records, subsequently began manufacture. Toxicity information was more frequently reported on PMNs that described nonpolymeric substances. That seems especially welcome, given that a near majority of PMNs have no toxicity information, because hazard is more often associated with nonpolymeric substances than with polymers (polymers are chemicals composed of repeating subunits).

These generally positive observations must be tempered by the fact that about half of PMNs reported no toxicity information. Furthermore, only 17 percent of PMNs have any test information about the likelihood of the substance's causing cancer, birth defects or mutations-three biological effects that were singled out for special concern in TSCA.

The conclusions to be drawn from the results of the analysis presented here must be limited to generalizations about the frequency of submission of information. The results show that more data are reported for some classes of PMNs than for others.

The following chapters present the results of OTA's analysis of the technical content of PMNs and, where appropriate, related findings and conclusions. However, the *interpretation* of the results is not a matter of inherent validity or of one interpretation's being correct and others being wrong. Instead, the interpretation to be placed on the results will depend on the beliefs and outlook of the reader.

If the reader is of the opinion that no premanufacture reporting should be required or that only the information items specified in TSCA should be submitted, the results may be interpreted to show that the PMN program is resulting in too much information being submitted. If, on the other hand, the reader thinks that particular items of information other than the TSCA-specified items should be reported on every PMN, the results may be interpreted to show that too little information is being reported.

Considering the results in more detail may lead to a middle position. There is, as shown in this paper, a tendency for information to be submitted for substances likely to be more hazardous or to result in more widespread exposures. For instance,

toxicity data are submitted more frequently on PMNs that describe nonpolymers, which as a group are more likely to be hazardous, than on PMNs that describe polymers; more data are submitted on PMNs that describe consumer-use products than on other PMNs. Those observations are consistent with the idea that companies develop and report appropriate data to EPA.

The data that lead to the satisfying conclusion that more information is being reported about more worrisome groups of chemicals also show the frequency of toxicity data reporting. About 40 percent of nonpolymers scheduled for annual production in excess of 10,000 kg did not report any toxicity data. About 30 percent of PMNs describing nonpolymer, consumer use chemicals, to be made in amounts greater than 10,000 kg annually, did not report any toxicity. Taking a middle position might lead to the conclusion that the trends are encouraging, but attach reservations to conclusions about whether the information now reported is adequate for the review of all new chemicals.

Regardless of how the information about the frequency of submission of data is interpreted, immediate questions arise about whether the information available for a particular substance was appropriate and sufficient. Answering those questions would require an examination of EPA's decisionmaking process about at least some PMNs on a case-by-case basis. That study would be different from the one reported here, and would involve a process similar, in some regards, to that used by EPA to review PMNs. A group of scientists would review the data on the PMNs, supplement that information with other information available from the scientific literature and experts, decide if EPA's decision was appropriate, and ask whether additional information on the PMN might have made a difference in the decision.

The next two chapters discuss the regulation of new chemicals (ch. 2) and the methods used by OTA in this study (ch. 3). Chapters 4 through 6 present the results of examining PMNs for the reporting of TSCA-specified data items (ch. 4), of physical-chemical data (ch. 5), and of toxicity data (ch. 6). Chapter 7 presents comparisons of toxicity data reported on certain subgroups of PMNs (e.g. site-limited chemicals compared to all others and consumer-use chemicals compared to all others). Chapter 8 discusses actions taken by EPA to regulate new chemicals, and chapter 9 is a general discussion of the the OTA findings.

"New Chemicals" and the Toxic Substances Control Act

2. "New Chemicals" and the Toxic Substances Control Act

After more than 5 years of consideration and debate during three terms of Congress, the Toxic Substances Control Act (TSCA) was passed by Congress on September 28, 1976, and signed into law by President Ford on October 11,1976. TSCA states that it is Federal policy that: 1) chemical manufacturers and processors are responsible for developing data about health and environmental effects of their products, 2) that there be adequate statutory authority to regulate chemicals posing an unreasonable risk to health or the environment, and 3) that regulatory efforts not unduly impede innovation.

An important facet of TSCA (and the Resource Conservation and Recovery Act, which provides for the regulation of chemical disposal) is that the law directs regulatory emphasis at hazardous substances wherever they may occur. Other environmental protection laws are directed at regulating exposures through specific media, such as air and water.

TSCA is generally directed at chemical substances (TSCA sec. 2), and section 3 defines a "chemical substance" as any organic or inorganic substance of a particular molecular identity including any substance which results in whole or in part from a chemical reaction *or* that occurs in nature as well as any element or uncombined radical. [Note: Throughout this report the terms "chemical" and "substance" are used interchangeably to mean "chemical substance."]

Certain substances are excluded from regulation under TSCA:

- mixtures;
- pesticides, regulated under the Federal Insecticide, Fungicide and Rodenticide Act, when they are used as pesticides;
- tobacco and tobacco products;
- nuclear materials, which are regulated under the Atomic Energy Act;
- food and food products which are regulated under the Federal Food, Drug and Cosmetic Act; and
- pistols, firearms, revolvers, shells, and cartridges.

Section 5 of TSCA is directed at preventing human and environmental exposure to new substances that will present or may present an unreasonable risk to human health or the environment and requires that the Environmental Protection Agency (EPA) be notified before new chemicals are introduced into commerce. The requirement for premanufacture notice (PMN) reflects the conclusion that human health and the environment may be better protected at less cost when a toxic chemical is regulated before it has become established in commerce:

> The most desirable time to determine health and environmental effects of a substance, and to take action to protect against any potential adverse effects, occurs before commercial production begins. Not only is human and environmental harm avoided or alleviated, but the cost of any regulatory actions in terms of loss of jobs and capital investment is minimized. (TSCA Legislative History, p. 678, quoted in OTS, **1982).**

REGULATION OF NEW CHEMICALS

Premanufacture notification allows EPA to make regulatory decisions about "new" chemicals. The category of new chemicals was established by TSCA section 8(b), which directs the Administrator of EPA to compile an "Inventory of Chemical Substances" of all chemicals subject to the provisions of TSCA that are manufactured or imported into the United States. The Inventory

was published on June 30, 1979, and all chemicals that did not appear on that list and which are not exempted from TSCA, are, by law, new.

Section 5 of TSCA stipulates that any person who intends to manufacture a substance that is not listed on the inventory and that is not excluded from TSCA must notify EPA of his or her intention 90 days before manufacture is to begin. Manufacture of small amounts of a chemical for research and development purposes to determine its usefulness and properties is, of course, permitted.

To initiate the EPA review of the new chemical, the company submits a PMN that is to contain information about chemical identity, proposed uses of the chemical, the expected production volumes of the chemical for various uses, expected byproducts, estimates of the numbers of people likely to be exposed in manufacture of the chemical, and methods for disposal.

> The notice . . . shall include—
>
> (A) insofar as known to the person submitting the notice or insofar as reasonably ascertainable, the information described in subparagraphs (A), (B), (C) (D), (F), and (G) of section 8(a)(2), and
>
> (B) in such form and manner as the Administrator may prescribe, any test data in the possession or control of the person giving such notice which are related to the effect of any manufacture, processing, distribution in commerce, use, or disposal of such substance or any article containing such substance, or of any combination of such activities, on health or the environment, and
>
> (C) a description of any other data concerning the environmental and health effects of such substance, insofar as known to the person making the notice or insofar as reasonably ascertainable. (TSCA sec. 5(d)(1)(a))

The subparagraphs of section 8(a)(2) referred to in section 5(d)(1)(a) read as follow:

> (A) The common or trade name, the chemical identity, and molecular structure of each chemical substance or mixture for which such a report is required.
>
> (B) The categories or proposed categories of use of each such substance or mixture.
>
> (C) The total amount of each substance and mixture manufactured or processed, reasonable estimates of the total amount to be manufactured or processed, the amount manufactured or processed for each of its categories of use, and reasonable estimates of the amount to be manufactured or processed for each of its categories of use or proposed categories of use.
>
> (D) A description of the byproducts resulting from the manufacture, processing, use or disposal of each such substance or mixture.
>
> (F) The number of individuals exposed, and reasonable estimates of the number who will be exposed, to such substance or mixture in their places of employment and the duration of such exposure.
>
> (G) ., . the manner or method of its [such substance or mixture] disposal . . . (TSCA sec. 8(a)(2)).

ACTIONS AVAILABLE TO EPA FOLLOWING PMN REVIEWS

The Administrator of EPA is charged with reviewing the information in the PMN within 90 days after receipt of the notice, and the agency can extend that review period for a maximum of 90 additional days (TSCA sec. 5(c)). The review of a PMN can result in any one of at least four actions by the agency.

(1) If the data in the PMN and expert opinion within the agency do not lead to the conclusion that an unreasonable risk is associated with the substance, manufacture can begin without restriction. Importantly, if EPA takes no action and the Agency is notified that manufacture of the substance described on the notice has begun, the name of the substance is placed on the Inventory of Chemical Substances. Unless the substance is the subject of a Significant New Use Rule (SNUR), this action transfers the substance from the "new" category, subject to section 5 of TSCA, to the "existing" category. [A "SNURed" chemical (see (2) immediately below) remains subject to section 5 requirements.] The testing and regulation of existing chemicals are the subject of other sections

of TSCA. Those sections are not discussed in this report.

(2) If EPA decides that the manufacture and use of the substance as described in the PMN are not associated with unreasonable risk, but, that a potential new use of the substance might be associated with unreasonable risk, EPA can commence a separate rulemaking to restrict the manufacture or distribution of the substance for uses not specified in the PMN. Under such a rule, manufacture can commence for the particular uses named in the PMN, but if the company that submitted the PMN or any other company decides to manufacture the substance for a "significant new use," EPA must be informed. The Agency then can require additional information about the substance (TSCA, sec. 5(a)(1)(B)).

The use of this authority is illustrated by the example of a chemical developed for use in commercial cleaning compounds. EPA was satisfied that its use by professional cleaning people would not be associated with an unreasonable risk, but the Agency was concerned that its use by consumers might result in such a risk. EPA took no action against the manufacture of the substance for commercial uses but drafted a "consent 5(e) order" (see (3) immediately below) that requires the reporting of additional information about toxicity before the substance is manufactured for a new use. The submitter consented to the order and agreed not to contest it in court so that manufacture for commercial uses could begin. At the same time, EPA announced that it would write a SNUR that requires that the Agency be notified before the substance is manufactured for use in consumer products. Therefore, the name of the substance is placed on the Inventory of Chemical Substances but flagged so that any subsequent manufacturer will know it is subject to pending regulation. According to EPA officials, future 5(e) orders of any kind will generally be linked to SNURS unless the submitter withdraws the PMN in the face of the 5(e) order.

(3) Section 5(e) of TSCA authorizes EPA to issue an administrative order regulating a new substance pending development of additional information by the submitter. To issue a 5(e) order, EPA must make two findings: First, the information available to EPA is insufficient to permit the evaluation of any risk that maybe associated with the new substance, and, second, either the new substance may present an unreasonable risk to health and the environment or the new substance will be produced in substantial quantities, resulting in significant exposure.

> (1)(A) If the Administrator **determines that**
>
> **(i) the information available to the Administrator is insufficient to permit a reasoned evaluation of the health and environmental effects of a chemical substance with respect to which notice** [PMN] is required . . . ; and
>
> (ii) (I) in the absence of sufficient information to permit the Administrator to make such an evaluation, the manufacture, processing, distribution in commerce, use, or disposal of such substance, or any combination of such activities, may present an unreasonable risk of injury to health or the environment, or
>
> (11) such substance is or will be produced in substantial quantities, and such substance either enters or may reasonably be anticipated to enter the environment in substantial quantities or there is or may be significant or substantial human exposure to the substance,
>
> the Administrator may issue a proposed order . . . to prohibit or limit the manufacture, processing, distribution in commerce, use, or disposal of such substances or to prohibit or limit any combination of activities (TSCA, sec. 5(e)).

In practice, 5(e) orders require that the PMN submitter develop specific items of information to assuage EPA's concern about the substance. The order can either prohibit or restrict manufacture during the period required for the development of additional information.

(4) Finally, EPA may decide from examination of the PMN that the manufacture, processing, distribution, use, or disposal of the substance "presents or will present an unreasonable risk of injury to health or environment" (TSCA sec. 5(f)). In those cases, EPA can regulate the substance.

Briefly, then, EPA can make any one of four decisions after inspecting a PMN:

1. The substance described on the PMN can be manufactured without restriction.

2. The substance can be manufactured for the uses described on the PMN, but the Agency can require that it be notified if manufacture for a significant new use is considered (TSCA sec. 5(a)(2)).
3. The manufacture, processing, distribution, use, or disposal of the new substance can be regulated pending the development of additional information about the substance (TSCA sec. 5(e)). In these cases, the Administrator must conclude that a decision about unreasonable risk cannot be made because of missing information.
4. The manufacture, processing, distribution, use, or disposal of the new substance can be regulated because it presents or will present an unreasonable risk (TSCA sec. 5(f)). In these cases, the Administrator decides that the available information is sufficient to decide that regulation is required.

PUBLIC NOTICE OF NEW CHEMICALS CONSIDERED FOR MANUFACTURE

TSCA section 5 (d)(2) provides that the Administrator is to publish a notice of receiving a PMN in the *Federal Register* within 5 business days after receipt of the notice. The published notice is to: 1) identify the chemical substance, 2) list the uses or intended uses, and 3) describe the results of any tests that were required by EPA rules under the provisions of TSCA section 5(b). (To date, no PMN containing EPA-required test results has been submitted.)

To protect confidential business information (CBI) from **public disclosure,** the submitter may designate those information items in a PMN that, were they to become public, would harm the submitter's business. Frequently, submitters have designated the chemical name as CBI. In those cases, the submitter, as part of the PMN, can use EPA guidelines and propose up to three "generic names" for listing in the *Federal Register.*

PMN REPORTING REQUIREMENTS

As required by TSCA section 5 (d)(1) all PMNs shall contain sufficient information to identify the new chemical, and to describe its projected uses and production volume, the number of workers likely to be exposed to it, its byproducts, and methods for its disposal. Those information items are specifically identified in the Act. In addition, TSCA section 5 lists some general classes of information that are to be reported on the PMN. The general reporting requirements say that any available information about the substance's physical and chemical properties and effects on health and the environment are to be included.

EPA has wrestled with the problems of specifying the form for PMNs and exactly what information should be submitted. In general, initial plans favored the submission of more detailed information, and subsequent modifications have pulled back to more general reporting requirements (see 44 F.R. 2242, Jan. 10, 1979; 44 F.R. 28564, May 15, 1979; 44 F.R. 59764, Oct. 16, 1979; 45 F.R. 74378, Nov. 7, 1980)

Currently, the EPA Office of Toxic Substances (OTS) is considering a proposal that PMNs will be required to contain only the items of information—chemical identity, proposed categories of use, estimates of production volumes, description of byproducts, estimates of the number of individuals exposed in their places of employment, and disposal methods—specified in TSCA section 5(d)(l)(a) and other "information that is essential for the review of most PMN's" (OTS, 1982). The other essential information is not described in *Priorities for OTS Operation,* but the point is made that even without having asked for additional information on the PMN itself, EPA will be able to telephone the submitter to ask for additional information as needed to review the

PMN. EPA states that in most cases, submitters have been forthcoming with such information when requested (OTS, 1982).

EPA also intends to require that all PMNs be submitted on a specified, simplified form (OTS, 1982). Currently, a PMN can be submitted on a form proposed by EPA, or on a form prepared by the Chemical Manufacturers Association, or on forms devised by individual companies.

EPA MANAGEMENT OF PMN REVIEW

Upon receipt of a PMN, EPA initiates a review that, with some exceptions, must be completed within 90 days. During the review period, EPA examines the PMN, and may request additional information from the submitter. If EPA does not find that the new substance presents or may present an unreasonable risk, EPA takes no action and the company submitting the PMN can begin manufacture when the 90-day period is completed. The submitter can request that the "clock be stopped" during the 90-day period if the company needs more time to develop information. If EPA agrees to the request, the agency waits until the company has obtained the desired information and then restarts the clock. Section 5(C) of TSCA authorizes EPA to extend the review period an additional 90 days for good cause.

PMN review is divided into 2 stages, an initial "screening" review and a detailed review. During the initial screening period, employees of EPA qualified by education and experience for the tasks, review the PMN for:

1. completeness, i.e., having the specific information required by TSCA;
2. correctness of chemical identity;
3. possibilities of occupational, environmental, and consumer exposures;
4. potential for human health effects;
5. potential for environmental effects; and
6. probable accuracy of projections of market size, new markets, and production volumes.

If an EPA reviewer thinks that the company might have additional information or that additional information is essential for the review, EPA can call the submitter. According to EPA officials and to some chemical company officials who reviewed the first draft of this OTA background paper, companies generally respond to such requests and supply the information.

When the requested information is unavailable or the company does not produce it, EPA employees can take one of several actions. They can make reasonable worst case estimates about the missing information, or they can negotiate with the company and reach an agreement that the company will run tests and supply data to EPA. If the company refuses to carry out necessary tests, EPA can write an order, as described by TSCA section 5(e), limiting or prohibiting manufacture pending development of appropriate data.

In general, each individual reviewer's report is reviewed by other, senior EPA scientists at a series of meetings. These meetings discuss the chemical described in the PMN, the information submitted, what conjectures can reasonably be made based on similarities to other chemicals, and appropriate strategies to search the literature for information about similar chemicals. Appendix A reproduces the items that may be discussed at the Evaluation Meeting which is held near the end of the initial screening period. Information about these items can be made available in the PMN or it can be estimated by EPA. Test-generated data are more reliable than estimates, but, there may be many instances when estimates are necessary.

The process of PMN review changed in May 1982 (as is described below). However, for most of the PMNs examined by OTA, the major decision was made at the "disposition meeting. " These meetings, held at day 45, considered the reviewers' comments and the reports of the earlier meetings, and discussed outstanding matters. The meetings produced one of four decisions:

1. no further review was necessary,
2. the chemical was referred to another EPA office or to another agency for action because OTS had identified an exposure that might

be of concern to another office or agency but was not of concern to OTS, or
3. the PMN was referred for detailed review, or
4. the decision was made to initiate some follow-up action, such as the writing of an SNUR.

If the first or second decision was reached, a final disposition report was written, the submitter was notified that manufacture could begin at the end of the 90-day review period, and the PMN file was closed out. If the third or fourth decision was reached, the PMN was sent to other groups within OTS for detailed review or other action.

Somewhat less than 10 percent of PMNs (7 percent of those examined by OTA) are sent to detailed review. Detailed review involves other individuals, frequently contractors to EPA, taking longer, harder looks at PMNs. During the detailed review, EPA can also telephone the submitter and request additional information. The EPA's *PMN Review Process Manual (OTS,* 1981) describes the review process in detail, and Arthur and Garrett (1982) provide a useful diagram of the process.

The review process was characterized by several EPA employees as reviews of reviews of reviews. There was agreement that the available information was thoroughly analyzed and that reasonable use was made of information about related chemicals. However, some EPA employees expressed concern about the adequacy of the data received on the PMNs and whether calls for additional information should have been made more often.

During the evolution of the PMN review process at EPA, some chemicals were identified as members of chemical classes that cause no or little concern about health or environmental effects. EPA scientists could, in the case of those chemicals, decide to drop them from further consideration at any time during the review period. In May 1982, the PMN review process was changed to accommodate EPA's conclusion that decisions about some chemicals could be made earlier in the review process. Since that time, a "focus meeting" has been held at about 15 days after PMN receipt. This meeting centers on identifying health and/or ecological concerns and assessing the accuracy of the estimates made of possible exposure to and release of the new chemical. The result of the focus meeting maybe a decision that the PMN describes a chemical of little or no concern, and such substances are dropped from further review.

OTA made no attempt to determine how the new meeting affected PMN review. EPA staff reported, however, that the meeting has been beneficial, speeded up the process, and conserved resources for the more difficult-to-review PMNs.

PROPOSED EXEMPTIONS TO THE PMN REPORTING REQUIREMENTS

TSCA section 5(h)(4) permits the Administrator of EPA to exempt substances from the PMN reporting requirements. The first exemption was granted on November 3, 1981, for chemicals used in or for instant photographic film articles (40 F.R. 54585). A manufacturer of those chemicals had petitioned for the exemption because of industry desire to introduce chemicals quickly in order to capitalize on newly opened-up markets. The 90-day PMN review period, according to the petition, would sometimes cause introduction of a new film to be delayed to the extent that a holiday market was missed. The exemption imposes requirements on the manufacture and use of the chemicals to restrict exposures.

On August 4, 1982, EPA proposed more general exemptions directed at:

1. site-limited intermediate chemicals,
2. chemicals manufactured in quantities of 10,000 kg (22,000 lb) or less annually, and
3. polymers.

The proposed exemptions for site-limited intermediates and low-volume substances were published in one notice (47 F.R. 33896), and the one for polymers was published separately (47 F.R. 33924).

EPA, in proposing these exemptions, responded to industry petitions that were based on two dif-

ferent lines of reasoning. Industry advanced the ideas: 1) that low-volume chemicals and site-limited intermediates are "characterized by limited exposure," and 2) that polymers "represent a class of substances that have intrinsically low levels of biological activity" (OTS, 1982).

Following some provisions of the industry petition, EPA proposed a policy that PMNs describing low-volume chemicals and site-limited intermediates that are not excluded from the exemption (see table 1) should be subject to an abbreviated EPA review. Agreeing with the idea that some polymers have inherently low toxicity, EPA decided that a finding of no unreasonable risk for those polymers would not depend on conditions of use, and that it would not be necessary for the Agency to review the specific properties or uses of certain polymers before they were manufactured (OTS, 1982). For certain other polymers, the Agency proposes a short review period (see table 2).

The proposed exemption for low-volume chemicals is divided into two parts. The first deals with substances made in amounts of 1,000 kg or less annually; the second with substances made in amounts of 10,000 kg or less annually. Any substance made in quantities of 1,000 kg or less would be granted an exemption unless under the conditions of use, the:

> . . . substance or a reasonably anticipated metabolite or environmental transformation product may cause . . . . serious chronic effects, including carcinogenic and teratogenic effects . . . . serious acute effects [lethal or sublethal] . . . . [or] . . . . significant environmental effects . . . under anticipated conditions of manufacture, processing, distribution **in commerce, use, or disposal.**

Table 1 .—Proposed Low-Volume and Site-Limited Intermediate Exemption Provisions

Exemption category*	Imports eligible?	Qualified expert review?	Exclusions (automatic)	Exclusions (under conditions of use)	Subsequent exemption notice required	Other manufacturers eligible for exemption?
Low volume (<1,000 kg)	Yes	No	None	Serious acute or chronic effects; significant environmental effects.	Before use or site of manufacture changes.	No
Low volume (<10,000 kg)	Yes	Yes	Carcinogenic or teratogenic effects. Acutely toxic effects.	Serious acute or chronic effects; significant environmental effects.	Before use or site of manufacture changes.	No
Site-limited intermediates	No	Yes	Carcinogenic or teratogenic effects.	Serious acute or chronic effects; significant environmental effects.	Before volume increases or site of manufacture changes.	Yes

*Some new chemical substances may be eligible for more than one exemption, Manufacturers and importers may apply for any exemption for which they are eligible.

SOURCE: Environmental Protection Agency; 47 F.R. 33897.

Table 2.—Proposed Polymer Exemption Provisions

Polymers for which no review is required	Polymers that qualify for a 14-day reveiw	Polymers excluded from exemption
1. Polymers manufactured from monomers listed by EPA. 2. Polymers of average molecular weights greater than 20,000. 3. Polymers that have limited and defined numbers of low molecular weight components.	1. Polymers of greater than 1,000 molecular weight.	1. Water soluble polymers. 2. Polymers containing less than 32 percent carbon. 3. Polymers containing more than specified percentages of certain elements. 4. Polymers produced by living or once-living organisms or cells ("biopolymers"). 5. Polymers containing halogens or cyano groups. 6. Polymers containing chemically reactive groups. 7. Polymers that are designed to degrade, decompose, or depolymerize.

SOURCE: Office of Technology Assessment from Environmental Protection Agency; 47 F.R. 33924.

98-826 0 - 83 - 4

Chemicals suspected to have carcinogenic or teratogenic potential are to be automatically excluded from the proposed exemptions for site-limited intermediates and substances to be made in amounts between 1,000 and 10,000 kg annually. In addition, substances with potential acutely toxic effects are to be excluded from the 1,000 to 10,000 kg annually low-volume exemption. To be excluded from both the two proposed low-volume exemptions and the proposed site-limited intermediate exemption are any substances which, under conditions of use, potentially may cause serious acute or chronic health effects or significant environmental effects (table 1).

The reporting requirements for substances made in amounts between 1,000 and 10,000 kg annually or for use as site-limited intermediates include a stipulation that a "qualified expert" review all available data about the substance. The qualified expert, an employee of the submitting company or a consultant hired by the company, after his or her review, must conclude that the chemical meets the terms of the exemption.

To allow EPA to make a determination about the likelihood that a substance for which an exemption is requested will not cause an undesirable human health or environmental effect, the manufacture must submit a notice to the Agency 14 days before commencement of manufacture that states which exemption is being sought. In addition, for substances to be manufactured or imported in amounts of 1,000 kg or less annually, the notice is to contain sufficient information to identify the chemical and describe its use and site of manufacture. EPA, on the basis of toxicity data or by reason of structural analogies between the substance proposed for exemption and known toxic substances, could declare the chemical ineligible for exemption.

For substances to be made or imported at between 1,000 and 10,000 kg annually and for site-limited intermediates, the notice is to contain information about chemical identity, description of uses (for low-volume chemicals), production volume (for site-limited intermediates), and site of manufacture. EPA can declare any substance ineligible for exemption if the notice fails to meet the exemption requirements. Substances that are granted exemptions are not eligible for listing on the Inventory of Chemical Substances and remain subject to PMN requirements.

As is shown in table 1, only the first company to submit an exemption for low-volume production will be eligible for exemption. If, subsequently, another submission is made for a chemical that has received a low-volume exemption, a complete PMN and review will be required. A trade association that reviewed the first draft of this report objected to this provision of the proposed exemption. They argue that any number of manufacturers should be eligible for low-volume exemption from PMN reporting requirements on a chemical. Any number of manufacturers can receive a site-limited exemption to manufacture a substance.

The proposed polymer exemption distinguishes between polymers for which no review is required, those for which a 14-day review is required, and those excluded from exemption. Table 2 displays some aspects of the polymer exemption.

Polymers exempted from any review will require only that EPA receive an exemption notice at the time of the start of manufacture. Such substances will not be entered on the Inventory of Chemical Substances because they have not undergone PMN review. The exempted polymers will become subject to section 5 PMN requirements if manufactured outside the terms of the exemption.

For polymers subject to 14--day review, a PMN must be submitted to EPA that identifies the manufacturer, the site of manufacture, and the polymer, and provides information about the molecular weight of the polymer and the amount of low-molecular weight material in the polymer preparation, projections of expected production volumes and uses, and any test data. Furthermore, the submitter must certify that the substance is a polymer and that it meets the conditions for exemption.

In the event that EPA does not notify the submitter otherwise, manufacture of the polymer can begin at the end of the shortened review period. Manufacturers are to notify EPA when manufacture commences, and, at that time, a polymer that has completed the 14-day review and gone into

production will be placed on the Inventory of Chemical Substances.

Certain classes of polymers (table 2) are excluded from the proposed exemption rule. In general, EPA excluded those classes because the agency has not had sufficient experience with them to accept that they are of low potential hazard.

The low-volume, site-limited intermediate, and polymer exemptions are still in the proposed stage. Objections to the proposed exemptions focus on the undeniable fact that less information would be received by EPA about the exempted substances and that EPA's review period would be shortened. EPA justified its decisions on the basis that the proposal exemptions are sufficient to guard against unreasonable risk. However, several comments have been received arguing against the exemptions because they are seen as weakening the PMN process to the point that protection against unreasonable risks is being lessened. On the other hand, industry sees the proposed exemptions as having ample safeguards and argue that the procedure should be further simplified to minimize burdens.

Several reviewers of the first draft of this background paper objected to the proposed exemptions. The exemption categories are seen as being too broad. The absence of a requirement that the qualified expert submit the data considered in reaching a decision to certify a substance as qualified for exemption is viewed as preventing EPA from carrying out its duty to review test data before a chemical is manufactured. Furthermore, some reviewers expressed concern that polymer preparations may be contaminated with hazardous chemicals and that EPA's general decision that some polymers are inherently less hazardous is an unjustified overstatement.

RISK ASSESSMENT

Two factors are of importance in estimating the risk that may be posed by a substance. The first is to determine any deleterious effect that the substance may cause to human health or the environment. In this background paper, the word "hazard" will be used to describe such effects. The second factor is "exposure."

Exposure is a complicated factor; determining it for risk assessments considering human health involves estimating the number of people who may come in contact with the substance, the duration of the contact, the route(s) of adsorption, the amount of substance which may be encountered by people, and, especially for workers, whether or not they employ personal protection equipment to reduce the contact. For environmental risk assessments, exposure estimates must consider the number and kinds of organisms that might come into contact with the substance and the distribution of the substance in different parts of the environment. An additional complicating factor in considering exposures is the persistence of the substance, which may vary in different parts of the environment.

Human risk is estimated from knowledge of the health hazard of a substance and the number of people who are likely to be exposed to it at particular exposure levels (9). Environmental risk is estimated from knowledge of the environmental hazard of a substance and the number of organisms or fraction of the environment expected to come into contact with the substance at expected exposure levels.

Low levels of either hazard or exposure reduce the amount of concern expressed about a substance. For instance, a very hazardous toxic substance might be used in manufacturing. Although its toxicity is well known, the chemical is also contained in sealed reaction vessels and there is little or no human or environmental exposure. While there is some lingering concern in case an accident releases the chemical, safeguards to contain the accidental release or inactivate the chemical can reduce those worries also. Limited exposure, then, reduces concern about risks.

At the other extreme are substances to which exposure is widespread but which have extremely low toxicities. For instance, polyester fibers in

clothing, to which almost everyone is exposed, cause no worry for the population in general because of very low (if any) toxicity.

EPA, or any other risk assessor, needs information about both hazard and exposure. If either hazard or exposure is very low, the need for the other kind of information maybe reduced. However, always, both components of risk must be considered. This background paper reports the frequency with which PMNs contained information useful in making risk assessments.

EPA has to estimate effects when toxicity data are not included in the PMN. The technique for making those estimates and some difficulties with it are described in the next section.

STRUCTURAL ACTIVITY RELATIONSHIP ANALYSIS AND ITS USE IN PMN REVIEW

Only about half of PMNs report any toxicity data (see ch. 6), and although about 96 percent report at least one physical-chemical datum in addition to those specified in TSCA, reporting of such data is spotty (see ch. 5). EPA, in the absence of those data, must estimate either toxicity or physical-chemicals properties. A complex of activities—examining the chemical structure of the new substance, deciding which parts of the structure may be important in biological systems, comparing the structure to related structures described in the chemical literature, and making projections about the toxicity or chemical behavior of the new substance—is involved in making estimates when data are lacking. All of these activities are grouped under the rubric of Structural Activity Relationship (SAR) analysis.

The underpinnings of SAR analyses are many observations that certain chemical structures and subunits are associated with toxic properties and other structures and subunits are not. At the same time, it is well known that some substances which are quite closely related differ significantly in toxicity. A well-known example is the comparison of 2-acetylaminofluorine to 4-acetylaminofluorine. These two substances differ in the location of a small chemical sidechain; the first is a carcinogen; the second is not. The very different toxic properties of these two similar chemicals points to the difficulties of using SAR (9).

No one claims that SAR is developed or refined to the point that no toxicity testing is necessary. However, arguments do arise about when its use is appropriate, when it leads or may lead to incorrect predictions about toxicity. Ideally, criteria for when it is and is not appropriate would be available, but they have not been developed. The considerable amount of professional opinion and considered judgment that are involved in the use of SAR analysis is illustrated in EPA's proposed low-volume chemical and site-limited intermediate exemptions.

> Factors that will be considered in evaluating structural similarity include the molecular size, shape, charge distribution, and weight, and the position, size, and chemical characteristics of functional groups or other substituents. These factors are judged in terms of their effect on such parameters as chemical reactivity, stemochemically governed interaction with enzymes, absorbability and distribution, metabolism, and excretion from an organism. (Other factors and parameters may be important in specific cases.) The greater the number of such factors that are identical or nearly identical between two substances, the closer the structural similarity.
>
> The absolute degree of structural similarity, however, is not the important determinant of the *significance of structural similarity* . . . . the significance of structural similarity to a human or animal carcinogen or teratogen would be judged with reference to the probability of eliciting carcinogenic or teratogenic effects. Therefore, all available information concerning possible mechanisms of action of a carcinogen or teratogen will be relevant to an assessment of the significant [sic] of structural similarities between that substance and a new chemical substance. Moreover, information indicating that certain groups on the carcinogen or teratogen are or maybe critical for toxicologic activity has to be considered before determining whether the new molecule has significant

structural similarity to a referent chemical. Structural similarities at toxicologically significant sites or a molecule are of greater importance than similarities at other sites.

In a number of cases, neither the mechanism of action nor structural requirements for activity of a referent toxic substance is known, even though its toxicity has been clearly established. In such instances, attention is usually drawn to chemically or biologically active groups as potential sites of action. Structural similarity at these sites would reasonably be accorded higher significance than similarity at less reactive sites.

It follows from this summary statement that *a determination of significant structural similarity is often dependent on the kinds and amount of toxicological information available for the referent chemical.* Because this information will vary for each new substance, the Agency is unable to prescribe definitive criteria against which structural similarity can be measured. The determination whether there is significant structural similarity will be based primarily on whether there is an identifiable or plausible mechansim [sic] of toxicity that can be shared by the referent chemical and the new substance; or, lacking information or hypotheses on mechanism, whether substructures known or expected to be required for activity of the referent chemical are present in the new **substance (47 F.R. 33900). (Emphasis added** in paragraphs 3 and 4).

An acknowledged shortcoming of SAR analyses is that it can say nothing about an entirely "new" structure. However, EPA officials point out that the vast majority of substances submitted on PMNs are derivatives of known chemicals and that SAR is useful and sufficient to make decisions about those.

It would be possible to compare PMNs that describe novel chemicals to those that describe "me too" chemicals with an eye to determining if more data, especially toxicity data, were submitted on substances for which SAR is more likely inappropriate. Such an analysis was beyond the resources of the study described in this background paper.

Questions can be asked about what criteria EPA used to decide that SAR was sufficient for making estimates of toxicity. OTA did not attempt to answer that question, but it is clear from data presented in this paper that in many cases no toxicity data were presented on the PMNs. In those cases, if EPA was concerned about toxicity, the Agency would have to rely on SAR. It may be that EPA was too willing to use SAR analysis when what was desirable or actually necessary was more information about the chemical. To determine whether or not EPA received necessary information about particular chemicals would require a study different from the one described here (see ch. 9).

3 ■

Methods Used in Study of Information Content of Premanufacture Notices

3. Methods Used in Study of Information Content of Premanufacture Notices

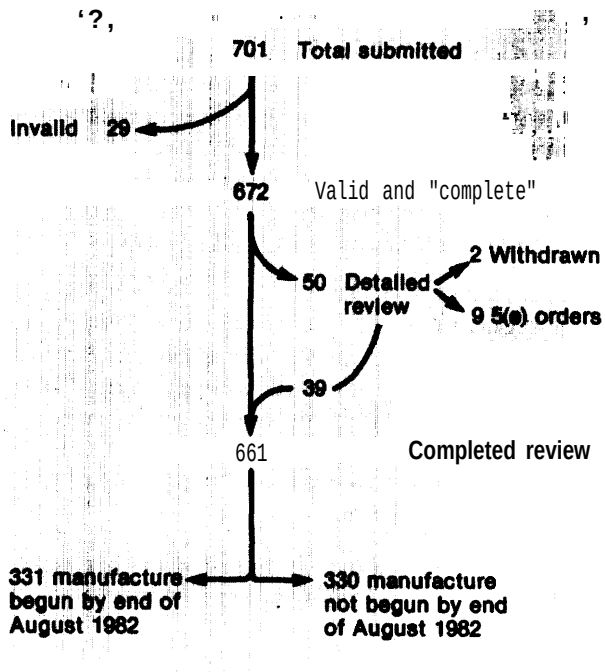
PMNS EXAMINED BY OTA

All premanufacture notices (PMNs) considered by the Environmental Protection Agency (EPA) to be valid and complete that were received by EPA from the beginning of the program (July 1, 1979) through the end of June 1981 and which either completed PMN review *or* were withdrawn because of a 5(e) notice being planned *or* written were examined. In addition, the PMNs submitted in June 1982 were examined by OTA. The total number of examined PMNs was 740; 670 of which were received in the first 2 years of the program and 70 of which were received in June 1982.

Figure 2, which is based on records obtained from EPA, describes the disposition of the 701 PMNs that entered review through June 1981. Twenty-nine of the PMNs were returned to the submitters as invalid; some of these PMNs described chemicals already on the Inventory of Chemical Substances, and no PMN was necessary for them. Others of the invalid PMNs were judged to be incomplete.

Of the 672 valid PMNs, 50 underwent detailed review, indicating that additional review was necessary to resolve some uncertainty about risk that remained after the initial screen. Nine of the fifty were associated with unreasonable risk during the detailed review, and 5(e) orders were written. In each of those nine cases, the submitters abandoned their intent to manufacture or import the new substance and withdrew the PMN rather than perform testing. In the case of two other PMNs that underwent detailed review, the manufacturers decided to withdraw the PMNs before a 5(e) order was written. The remaining 39 PMNs that underwent detailed review PMNs *were* either: 1) judged not to present an unreasonable risk or 2) judged not to present an unreasonable risk because the submitters undertook voluntary actions to reduce hazard or exposure after EPA informed the submitters of agency concern.

Figure 2.—Disposition of PMNs Submitted From July 1979 and Including All Those That Completed the 90-Day Review Period by the End of September 1981



SOURCE: Office of Technology Assessment from data collected by the Environmental Protection Agency,

Mr. Florio's letter (fig. 1) requesting this study specifically asked that OTA compare PMNs describing marketed (manufactured) chemicals to those that described chemicals that have not been manufactured. OTA used EPA-compiled records to separate the PMNs received through June 1981 into those that had been manufactured by August 1982 and those that had not.

Some EPA employees told OTA staff that there is no legal requirement that a submitter report that manufacture has begun and that separating the PMNs between those that described chemicals that

98-826 0 - 83 - 5

have begun manufacture and those that have not may be subject to significant error. However, EPA encourages submission of a "notice of commencement" (NOC), and industry reviewers of the first draft of this study firmly expressed their opinion that NOCs were viewed as a required notice and that they were submitted. OTA depended on EPA's classification of a chemical as being manufactured or not, which in turn depended on the Agency's having or having not received an NOC. There maybe some error in those classifications. EPA was in the process of sorting out its NOC records when OTA **was** examining PMNs, and three different lists of manufactured chemicals were produced during that time. Some 40 chemicals listed as "manufactured" on EPA's first list were removed from subsequent lists because clerical or transcriptional errors at EPA had incorrectly classified them. OTA used the most recent available information from EPA, which should have the fewest errors in classification.

As is shown on figure 2, half of the PMNs that were received by EPA through June 1981 were classified as being manufacturered by August 1982. Therefore an examination of all the PMNs received by that date provides a comparison between 331 chemicals that were reported to have begun manufacture after EPA's receiving a PMN and 330 that had not.

The PMNs received through June 1981 that described the nine substances that did not proceed to manufacture because of EPA writing 5(e) orders were also inspected. In those nine cases, EPA decided that it had insufficient information to make a decision about unreasonable risk to human health or the environment and required that the submitters generate more data before manufacture could begin. In each of those cases, the submitters decided not to produce additional data, review was suspended as incomplete, and the substance did not begin manufacture.

In addition to the PMNs received through June 1981, the PMNs received in June 1982 were examined. Comparison of the PMNs received during the two time periods was expected to reveal any differences in PMN content between the 1979 to mid-1981 period and June 1982.

A shorthand nomenclature has been adopted to distinguish between and among the groups of PMNs examined by OTA. Those PMNs that were received through June 1981 and that described chemicals that had begun manufacture before the end of August 1982 are called "manufactured PMNs." Those that were received through June 1981 and that had not begun manufacture by August 1981 are called "nonmanufactured PMNs." All PMNs received in June 1982 are called "June 1982 PMNs." The nine PMNs for which EPA wrote 5(e) orders during the period 1979 through September 1981 are called "regulated PMNs."

INSPECTION OF PMN FILES

PMNs are submitted either on an EPA-provided form (44 F.R. 59764 and see app. B), on a form developed by the Chemical Manufacturers Association (CMA) (see app. B), or in other formats including letters. Upon receipt, each PMN is photocopied and distributed to the appropriate review groups in EPA. One copy is maintained in the document control room until the 90-day (or, in exceptional circumstances, longer) review period is completed, and a copy is then deposited in an inactive document control room.

In most cases, each inactive PMN is stored in a file folder along with additional information produced and obtained during EPA's review. During OTA's examination of PMNs, 11 file folders were empty. Because the original PMN documents were being photographed at a location away from EPA during the summer of 1982 when OTA was carrying out its examination, no copy of those 11 PMNs was available to OTA. Unless those 11 PMNs are included in the 29 "invalid" PMNs shown on figure 2, those PMNs are not included in any tabulation of PMNs reported here.

An annoying filing habit hampered OTA's inspection of some PMNs (and would hamper any other inquiry as well). Frequently, manufacturers

submit several PMNs at the same time. Sometimes the PMNs submitted together are closely related; for instance, two forms of an organic chemical differing only in that one is a sodium salt and that the other is a potassium salt. Other times, the PMNs submitted together have nothing in common except that they are the products and intermediates in a series of reactions. For instance, Chemical A+ Chemical B -> Chemical C. Putting such PMNs together in a single file results in the PMN forms being intermixed, and although separable by attention to numbers on the form, information retrieval is slowed.

OTA staff examined each PMN file for the presence or absence of information (45 items) and recorded findings on the form illustrated in figure 3. To a major extent, OTA's investigation depended on recording whether or not an item of information was present. Three reasons could account for OTA's reporting that no information had been submitted for an item:

1. The submitter had not presented the information.
2. The submitter had presented the information, but the information was not present in the file inspected by OTA.
3. OTA incorrectly recorded that no information was present.

There was no way to judge the frequency with which a piece of information was lost from a file (reason 2), but it was essentially impossible for a single item or a few items of information that were reported on a PMN to be lost. PMNs are stapled. Therefore, if any information reported on the PMN was found about a substance, probably all the PMN-reported information was found. However, some EPA staff mentioned to OTA that records of telephone conversations with submitters were sometimes lost from the files. Therefore, some information that was reported to EPA might have been lost from the files and not recorded by OTA. In fact, the concern expressed about lost telephone records was so great that even though the OTA data collection form provided for the tabulation of data requested by EPA subsequent to the PMN submission, those data were not analyzed separately. Instead, the presence of a datum was recorded whether it was submitted on the PMN or secured by a phone call during the review process.

OTA staff could have misreported the absence of information (reason 3 for OTA reporting that an item of information was not reported). Such errors are bound to occur, especially in an effort that includes collecting 45 pieces of information about 740 PMNs (a total of 33,300 pieces of information). To estimate the frequency of such errors, the information collected by OTA about whether each PMN described a Class 1, Class 2, or Class 3 substance was rechecked. Each of the 740 PMNs was reexamined to determine how frequently the class of the chemical reported on the notice was correctly recorded by OTA. That examination showed that 23 errors were made in 740 entries, or an error rate of 3 percent. (The data presented in this background paper report the corrected counts about chemical classes.)

INFORMATION COLLECTED FROM PMNs

The OTA data collection form (see fig. 3) was designed to facilitate recording of the presence or absence of information required by TSCA (see lower right hand comer of form) and the presence or absence of some data items identified by the Organization for Economic Cooperation and Development (OECD) as useful in reviewing the properties of new chemicals. Those data items, called the Minimum Pre-marketing Data (MPD) set, were accepted by the European Economic Community (EEC) as a common standard for the premarket review of many new chemicals and were considered for adoption as a mandatory reporting system by OECD. However, in a December 1982 meeting, OECD decided that reporting of the MPD data is only one way to provide information about the toxic effects of new chemicals. The United States, the only OECD member that did so, objected to the MPD requirement because it represented "inflexible, across-the-board, one-time notice requirements for all new chemicals," and EPA, which represented the

Figure 3.—Form Used by OTA in Collection of Data From PMNs

PMN

File #_____ CMA__ OTHER___ EPA___ Date NOC Filed_/__/__ Time Difference Days

Parent Subsidiary— Manufacturer Feedstock Source Sole Customer
Further Processor— Other—

Production Volume---Exemption___ Non-exemption___

Import___country_____ Non-import_____

Polymer_ Low Volume Site-limited___ Intermediate Other___

Final Disposition:

Specify any additional information requested: YES OR NO

OECD

CHEMICAL ID
Chemical Name
Formula
CAS#
Finger-print Spectra
Degree of Purity

PRODUCTION
Estimated Production/year
Intended Uses Ind. Corn Cons SL Inter
Disposal Methods
Mode of Transportation

RECOMMENDED PRECAUTION AND EMERGENCY MEASURES

ANALYTICAL METHODS

PHYSICAL DATA
Melting Point
Boiling Point
Density
Vapor Pressure
Water Volubility
Partition Coefficient
Hydrolysis
Spectra—
Adsorption-Desorption
Dissociation Constant
Particle Size

ACUTE TOXICITY
Acute Oral Toxicity
Acute Dermal Toxicity
Acute Inhalation Toxicity
Skin Irritation
Skin Sensitization
Eye Irritation

REPEATED DOSE TOXICITY DATA
14-28 Days

MUTAGENICITY DATA

ECOTOXICITY DATA
Fish LC_{50}-at least 96 hr exposure
Daphnia -reproduction 14 days
Alga -growth inhibition 4 days

DEGRADATION/ACCUMULATION DATA
Bio-degradation:
Bio-accumulation:

EPA, TSCA section 5 requirements:
Chemical Name and Structure
Intended Uses
Estimated Production Volume
Byproducts
#of Workers to be Exposed
Disposal Method
Toxicity

/=data present
XX=data absent

SOURCE:Office of Technology Assessment.

United States at the OECD meeting, prefers the more flexible PMN reporting requirements that have been developed under the Toxic Substances Control Act (TSCA) (3). In some cases, other items of information, neither specified by TSCA nor identified by OECD, were submitted on a PMN and those were noted by OTA on its forms.

The OTA form provided space to record the type of form used for the PMN submission and whether or not the substance had entered manufacture (NOC = "notice of commencement" of manufacture). In addition, OTA recorded whether or not the substance might be exempted from the usual PMN review under EPA's proposed low-volume, polymer, or site-limited intermediate exemption programs. These classifications on OTA's part were necessarily rough. If the PMN identified the substance as being made in amounts of less than 10,000 kg annually, or as a polymer, or as a site-limited intermediate, that information was recorded. Some of these chemicals might not fit into an exemption category because of reasons not reported on the PMN or recorded by OTA, and in some cases the submitter might prefer to submit a regular PMN rather than an exemption notice even if the exemption program were in effect. Nevertheless, the submitter-supplied information about production volumes, site-limited and polymer attributes allows some analysis of the information content of PMNs that describe members of classes being considered for exemption from PMN reporting requirements by EPA.

The "final disposition" indicated whether or not a 5(e) order was written for the substance. If there was a record of EPA-requested additional information, that was also noted in the form.

Data were transferred from the OTA form to a computer for analysis. The accuracy of the transfer of data was checked visually and corrections made before the analysis began.

SECURITY PRECAUTIONS TO PROTECT CONFIDENTIAL BUSINESS INFORMATION

EPA has to protect the confidential business information (CBI) that is included in PMNs. OTA staff who were to have access to PMNs signed a *security* agreement with EPA pledging not to divulge any CBI from the PMNs. In addition, OTA staff read the relevant parts of the EPA security guide dealing with protecting CBI. OTA made the suggestion that the first draft of this report would be first circulated to the appropriate security officials at EPA so that EPA could bring to OTA's attention any CBI that was included in the background paper. This agreement was modified somewhat. EPA security officials inspected all tabular data in the first draft for CBI. After they agreed that no CBI was in the tables, the draft was sent out for review. Furthermore, OTA staff agreed not to remove any PMN file or its contents from the workroom that was provided for OTA at EPA.

OTA's legal counsel informed OTA staff that none of these conditions was necessary for OTA to obtain and examine CBI. However, in the interest of being cooperative and because the restrictions that OTA agreed to did not greatly hobble OTA's work, OTA staff entered into the agreements mentioned above.

EPA COOPERATION

EPA staff *were* courteous and helpful to OTA staff throughout this project. Helpfulness was extended by EPA staff in day-to-day cooperation and interviews. Many, but probably not all, of the EPA staff who aided this study are listed in appendix C.

ANALYSIS OF THE DATA

A computer program written by John Bell was used to analyze the collected data. The OTA-collected data and the program for analysis will be made available on request to OTA.

ORGANIZATION OF THE PRESENTATION OF THE ANALYSIS

TSCA contains both specific and general reporting requirements. The items specifically required are listed in TSCA section 5 (d)(1)(a)(A). In brief, the submitter is required to name and describe the chemical, make projections of the expected uses and production volumes, estimate the number of workers who may be exposed to the substance, describe byproducts of the chemical's manufacture, and present methods for disposal of the chemical. The general reporting requirements (TSCA sec. 5 (d)(1)(a)(B) and (C)) state that the notice shall include "any test data in the possession or control of the person giving such notice" that bears on the effects of the manufacture, use, and disposal of the substance and a description of any data about health and environmental effects of the substance "insofar as known to the person making the notice or insofar as reasonably ascertainable. "

EPA has defined the terms "possession or control" and "known to or reasonably ascertainable" in the proposed PMN reporting rules (44 F.R. 2265):

> "Known to or reasonably ascertainable" means all information in a person's possession or control, plus all information that a reasonable person similarly situated might be expected to possess, control, or know, or could obtain without unreasonable burden or cost.
>
> "Possession or control" means in possession or control of the submitter, or of any subsidiary, parent company, or any company which the parent company owns or controls if the subsidiary, parent company, or other company is associated with the submitter in the research, development, test marketing, or commercial marketing of the substance .... Information is included within this definition if it is: (I) in the submitter's own files, (2) in commercially available data bases to which the submitter has purchased access, or (3) maintained in the files in the course of employment by employees or other agents of the submitter who are associated with research, development, test marketing, or commercial marketing of the substance.

The general reporting requirements apply to two kinds of information, those that describe the new substance and those that describe results of tests of the substance's possible toxic effects. The OTA data collection form (fig. 3) was used to collect data for this study.

OTA examined each PMN to determine how completely:

1. the TSCA-specified data items were reported,
2. what additional physical-chemical information, and
3. what toxicity information was reported.

Results of OTA's inspection of PMNs are presented in four parts. Chapters 4, 5, and 6 describe the amounts of the three types of information submitted. Chapter 7 discusses the amount of information present in subgroups of PMNs, including those subgroups that are likely to be exempted from PMN reporting requirements and those that are of interest because of consumer use.

4
Frequency of Submission of TSCA-Specified Data on Premanufacture Notices

4. Frequency of Submission of TSCA-Specified Data on Premanufacture Notices

The Toxic Substances Control Act (TSCA) specifies that a company that plans to manufacture or import a new chemical in the United States submit a Premanufacture Notice (PMN) to the Environmental Protection Agency (EPA). The PMN is to contain information that identifies the chemical, projects the amount of the chemical to be made for specified uses, estimates the number of workers involved in manufacture, and describes byproducts produced in the chemical's manufacture and methods for its disposal. The frequency with which TSCA-required information was submitted was examined on PMNs that:

1. had been submitted before the end of June 1981, completed review by the end of September 1981 and the manufacture of which had begun by the end of September 1982 (called here "manufactured PMNs"),
2. PMNs like those in 1 except that EPA had not been informed about commencement of manufacture through the end of September 1982 (called here "non-manufactured PMNs"),
3. all PMNs submitted in June 1982 (called here "June 1982 PMNs"), and
4. PMNs that have not completed review because EPA issued a "5(e) order" requiring submission of more information (called here "regulated PMNs").

NUMBERS OF PMNs SUBMITTED TO EPA

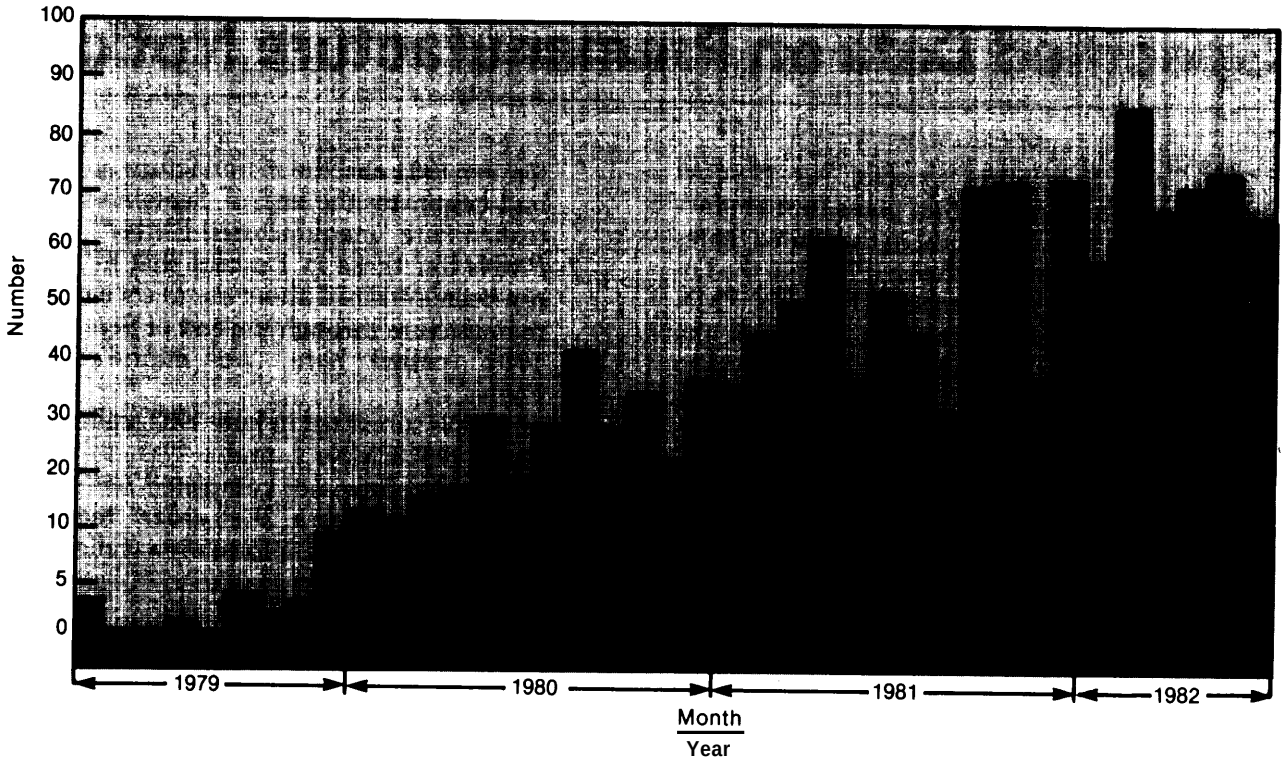
Figure 4 shows the numbers of PMNs received by EPA since the program's inception. As is readily apparent, the number of submitted PMNs was small at first, but rapidly increased. A number of factors might account for the increasing numbers of PMNs. It maybe that companies hastened the development process for new chemicals immediately before the start of the PMN program in order to list the chemicals on the Inventory of Chemical Substances without having to experience the delay and uncertainty of the PMN review process. That scheduling change could have contributed to a subsequent hiatus in the introduction of new chemicals. As a result of hurrying development of chemicals closest to production, the time necessary to complete development of chemicals at earlier stages might have been lengthened. Also, companies might have found it necessary to use the time when few PMNs were submitted to develop methods to prepare and submit the notices. Finally, any PMN-imposed additional burdens to develop and submit information might have caused a delay in submission of PMNs.

Although there is some flattening out of the rate of increase, the number of PMNs continues to increase. Since the beginning of 1982, EPA has received more than 70 valid notices each month.

It is important to remember that PMNs are required only for new substances. Many chemical products are formulations or mixtures of already existing chemicals, and those are exempted from the PMN reporting requirements by TSCA (see ch. 2). The number of new formulations and mixtures introduced each year was not determined by OTA, but it is certainly many times greater than the 1,000 or so new chemicals which require PMNs. Since the components of the mixtures and formulations are listed on the Inventory, they are subject to the provisions of TSCA that apply to existing chemicals.

98-826 0 - 83 - 6

Figure 4.–Number of Valid PMNs Received Each Month: April 1979 Through June 1982



SOURCE: Drawn from data collected by the Environmental Protection Agency.

CHEMICAL NAME AND PRODUCTION VOLUMES

Whatever is accepted about the usefulness and applicability of Structural Activity Analysis (SAR) (see ch. 2), it is clear that knowledge of the chemical's structure is central to the process of estimating chemical and biological properties. TSCA specifies that new chemicals be named and that formulas and structures be provided for chemicals when available. The reporting of these items is essential to review of the PMN.

Chemicals are named according to standard rules, and names, therefore, provide information about the substance. The name is a critical element in learning about the structure of the chemical, and, in turn, knowledge of the chemical's structure underpins EPA's review of the PMN. An accurate name is also necessary for listing the chemical on the EPA's Inventory of Chemical Substances at the end of the review period.

Essentially all PMNs report the chemical name (table 3). OTA's examination found 11 PMNs, a little more than 1 percent, that did not report a name. All of the PMNs that did not include names described polymers (see table 4).

The amount of the substance to be manufactured is an important element in estimating exposures. As is shown on table 3, essentially all PMNs report estimated production volumes. If EPA implements the program it is considering to exempt low-volume substances from PMN review, the estimates of production volume will take on additional importance.

Table 3.—Completeness of PMNs for TSCA-Specified Information

	Manufactured		Non-manufactured		June 1982		Regulated	Totals	
	Number	Percent	Number	Percent	Number	Percent	Number	Number	Percent
PMNs	331	100	330	100	70	100	9	740	100
Number with:									
Chemical name	325	98	326	99	69	99	9	729	99
Chemical class	331	100	330	100	70	100	9	740	100
Production volume	329	99	328	99	69	99	9	735	99
Uses	325	98	322	98	69	99	9	725	98
Byproducts	233	70	207	63	49	70	8	497	67
Number of workers	315	95	302	92	68	97	9	694	94
Disposal	313	95	298	90	65	93	9	685	93
All TSCA-specified information	218	66	190	58	46	66	8	462	62
All TSCA-specified information except by products	293	89	274	83	62	89	9	638	86

SOURCE: Office of Technology Assessment.

Table 4.—Number of Class 1, 2, and 3 PMNs That Have Name, Structure, and Formula

		Name		Formula		Structure		Formula and structure	
Class	Total	Number	Percent	Number	Percent	Number	Percent	Number	Percent
1	293	293	100	273	93	264	90	256	87
2	73	73	100	35	48	39	53	28	38
3	374	363	97	134	36	70	19	46	12

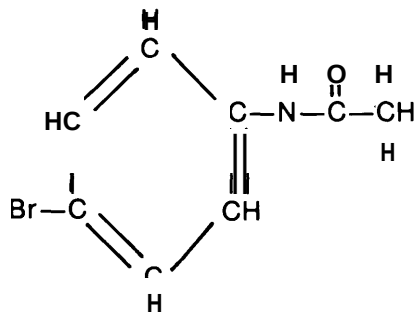
SOURCE: Office of Technology Assessment.

CHEMICAL FORMULAE AND STRUCTURES

EPA has divided all substances subject to regulation under TSCA into three classes. Essentially:

- Class 1 substances have a single component chemical and that chemical can be described by a chemical formula;
- Class 2 substances are complex combinations of chemicals, which cannot be described by a chemical formula; and
- Class 3 substances are polymers.

The EPA's proposed rule for PMN reporting (44 F.R. 59764) provides an example of a Class 1 substance. The name of the chemical in the example is N-(4-bromophenyl) acetamide; its formula, a listing of the atoms in the chemical, is C_8H_8ONBr; its structure is represented by a drawing that shows the arrangements and relationships of the atoms in the chemical:



Such precise representation is not possible for a complex combination of chemicals (Class 2), but knowledge of the components that go into the combination can sometimes be represented by formulae and structures.

Chemical polymers (Class 3) are chains of smaller chemicals. A linear homopolymer is a

chain of a single monomeric subunit. If the monomer is chemical A, the linear homopolymer is A-A-A-A-A-A . . . . Except for the fact that chain lengths may vary, say 50 or 100 or 500 or more As in different preparations, such a polymer can be represented accurately by structures and formulae.

Other polymers can have two or more different monomers, say B, C, and D, and their order of assembly may vary. For instance, a polymer made from a mixture of B, C, and D might be any of a great variety of polymers (. . . B-C-D . . ., or . . . D-B-B-B-C ..., etc.) that differ in composition and length. It is impossible to describe such heteropolymers by structures or formulae although each of the monomers can, of course, be so described.

Further adding to the complexity of polymers is that some branch. For instance, monomers E, F, and G might react to produce a backbone of E and F (. . . E-E-F-E-F . . .) with the G monomer being attached to all or some of the Es (. . . E-E-F-E-F ..., or . . . E-E-F-E-F . . .).

```
        |                    |   |
        G                    G   G
```

Few chemical reactions go to completion, and polymer preparations frequently have "unreacted" or "free monomers" associated with them. Sometimes the monomers are known to be toxic, and in those cases, knowing the percentage of free monomers or short polymers that is present is important.

As expected, given the relative ease of producing such information for Class 1 chemicals, 93 percent of Class 1 PMNs presented chemical formulae, 90 percent presented structures, and 87 percent both (table 4). The absence of this information from PMNs that do not report it may mean that the submitting company does not have the data.

Reporting of formulae and structures was much less frequent for Classes 2 and 3. As is shown on table 4, about half of Class 2 substance PMNs included either formula or structure and **38** percent included both. Industry and EPA reviewers of the first draft of this paper pointed out that information about the chemicals that were used in the reaction to produce a Class 2 substance frequently provides important data about the composition of such substances in lieu of formulae and structures. EPA reviewers further stated that the observed low frequency of reporting of formulae and structures for Class 2 substances produces a distorted view of the information the Agency receives on PMNs for those substances. The Agency reviewers expressed general satisfaction with the information submitted for Class 2 substances. Other reviewers expressed dismay about the absence of such information. And, again, a determination of what errors might have resulted from the absences would require a study of particular PMNs and the decisions made about them.

Of the PMNs for Class **3** substances, **36** percent included a formula, 19 percent a structure, and 12 percent both. If the name of the polymer is sufficient to indicate the identity of the monomeric subunits and their relationships, no further information may be necessary.

BYPRODUCTS

The TSCA-specified item least frequently reported on PMNs is the identification of byproducts produced during the manufacture of the new substance (table 3). Industry reviewers of the first draft of this paper pointed out that some reactions produce essentially no byproducts, and that the absence of information might reflect that no byproducts were present. While that may be the case, when a submitter reported that no byproducts were formed, that was recorded by OTA, and it is represented in the counts reported on table 3.

OTA examined the possibility that PMNs that described site-limited chemicals might more frequently not report byproduct information, and that excluding those from consideration might have a significant impact on the percentage of PMNs that report byproducts. However, 60 **(52** percent) of the 115 PMNs that described site-limited chemicals reported byproduct information. Therefore, although the percentage of site-limited PMNs that reported byproduct information was less than for all PMNs considered

together, excluding them from consideration would not materially affect the percentage of reporting of byproduct information.

The importance of byproducts **varies.** If the byproduct is a common chemical with no toxicity or if it is present in very low concentrations, it is of little or no concern. At the other extreme, the "dioxin" that is now of such concern because of health effects, is a byproduct of several manufacturing processes. A byproduct that is toxic or one about which little is known presents special problems. In any case, absence of reported byproduct identity decreases EPA's ability to evaluate any risk associated with the chemical's production and its byproducts.

USES

Uses for new chemicals are divided into three categories—consumer, commercial, and industrial-on the basis of information supplied by submitters on the PMNs. About three-fourths of all PMNs specified that the substance was intended for one or more of those classes of use. In addition, OTA counted those PMNs that described site-limited or intermediate chemicals as industrial-use chemicals. Adding that number of PMNs to the number that specified either consumer, commercial, industrial, or some combination of uses and to the 27 that described a general use substance, such as a component of a paint, brings the total of PMNs that reported uses to 725 (98 percent). (See table 3).

Exposure assessment depends on estimates of the numbers of people who may be exposed to **a** substance, on estimates of the amount of the substance that exposed persons may encounter, on estimated routes of exposure, and on estimates of incidence and duration of exposure episodes. Consumer-use products are most important in terms of numbers of people who may be potentially exposed to a substance. More people use them, and any restrictions placed on uses are more likely to be ignored or misinterpreted as the number of users increases. On the other hand, the highest potential intensity of exposure is likely for products used in industry for the fabrication of other products. Commercial-use products probably fall between consumer- and industrial-use products both in terms of number of people potentially exposed and in potential intensity of exposure. Table 5 shows that the most frequently reported uses were industrial, followed in order by commercial and consumer, and last, by general. Somewhat over **40** percent of all PMNs indicated that the chemical was expected to be used in more than one class of use (table 5).

Table 5.—Number of PMNs Describing Chemicals Intended for Industrial, Commercial, and Consumer Uses

Classes of use	Number of PMNs reporting use
Industrial	552
Commercial	247
Consumer	105
Industrial, commercial	111
Industrial, consumer	65
Commercial, consumer	66
Industrial, commercial, consumer	57
General	27

SOURCE: Off Ice of Technology Assessment.

NUMBER OF WORKERS EXPOSED AND DISPOSAL

Over **90** percent of all PMNs reported the numbers of workers who might be exposed and methods for disposal (table 3). Notes in the PMN files indicated that EPA had often called submitters to make inquiries about the numbers of workers estimated to be involved in the proposed manufacture of the substances described on the PMNs.

SUMMARY OF FINDINGS ABOUT REPORTING OF TSCA-SPECIFIED INFORMATION

Overall, 62 percent of the 740 PMNs reported all TSCA-required information. That low percentage of completeness is very much influenced by the low frequency of reporting byproduct information. When that item is ignored, 86 percent of PMNs reported all TSCA-specified information (table 3). It must be remembered, however, that byproduct reporting is TSCA-specified, and its frequent absence is remarkable. Production volume, chemical class, chemical name, and proposed uses were reported on almost every PMN. The number of workers potentially exposed to the substance and disposal methods were reported on over **90** percent of all PMNs.

The frequency with which TSCA-specified data was submitted did not differ by more than a few percent among the manufactured, nonmanufactured, and June 1982 PMNs. From OTA's examination, there is no discernible correlation between the likelihood of being manufactured and the completeness of submission of TSCA-specified information. Also there is no obvious change in completeness between the PMNs submitted through June 1981 and those submitted in June 1982.

TSCA specifies that the formula (atomic composition) and structure (arrangement of atoms) of a new chemical be reported when available. In practice, reporting formula and structure should be easiest for Class 1 substances. Class 2 substances, by definition, cannot be described by formula and structure although such information can be presented for components or reactants that were used to produce the complex composition substances of this class. Class 3 substances (polymers) also present problems for submitters; they may be of varying sizes and compositions. As expected, reporting of formula and structure was most frequent for Class 1 chemicals, 93 and **90** percent respectively. The same two items were reported on **48** and **53** percent of Class 2 PMNs; 36 and 19 percent Class of 3 PMNs (table 4).

The absence of formula and structure information on Class 2 chemicals would appear to create a weakness in PMN review, which often depends on knowledge of the structure of the substance. However, both industry reviewers and EPA reviewers of the first draft of this background paper are convinced that adequate information for review of Class 2 substances is present despite the absence of any formula or structure information from about half of the PMNs reporting those substances.

The absence of exact formulae and structures for polymers probably causes fewer problems. Polymers, because of their large size, tend to be inactive biologically. Concern may be attached to the monomers that are used to build the polymers, and ideally the formula and structure of the monomers should be included. Of course, concern about monomers decreases with decreasing concentrations of free monomers and short polymers in the polymer preparation. A more detailed analysis than that undertaken here would be necessary to determine if formulae and structures were submitted appropriately for polymers with significant monomer contamination.

OTA's finding that not all PMNs contain all items of TSCA-specified information does not square with EPA's classifying them as complete. In particular, information about byproducts was missing from more than **30** percent of the PMNs. It maybe that such information had been obtained by EPA during the PMN review process and subsequently lost from the files. If that is not the case, the absence of those data would necessarily complicate EPA's review.

5 .

Frequency of Submission of Physical-Chemical Information on Premanufacture Notices

5. Frequency of Submission of Physical-Chemical Information on Premanufacture Notices

Many different types of information can be used to describe the physical and chemical properties of a substance. The most important for the Environmental Protection Agency (EPA) are those that describe or project the behavior of the chemical under normal environmental conditions. For instance, a chemical that is soluble in water presents problems different from those of a water-insoluble chemical.

OTA inspected premanufacture notices (PMNs) for the presence or absence of nine items of physical and chemical information. Those nine are listed in table **6** along with a short description of the use of each item. Table **6** also lists two other items that were checked by OTA. "Transportation" provides information about how the chemical is to be moved, and "emergency information" means that the submitter has developed methods to cleanup spills and decontaminate workers who come in contact with the substance.

Inspection of appendix A shows that EPA evaluated many of these items of information in evaluating PMNs. When an item was missing from the PMN file, and it was of value to the PMN review, EPA scientists had to estimate it. The items examined by OTA include seven (melting point, boiling point, density, vapor pressure, volubility in water, partition coefficient, and infrared spectra) identified by the Organization for Economic Cooperation and Development as useful in describing new chemicals, and, at one time, recommended for inclusion in PMNs by EPA **(46** F.R. **8986).**

Table 6.—items of Physical-Chemical Information That Were Scored on PMNs

Item/Usefulness in determining possible risks of chemicals
Purity. -Necessary to delineate final product composition and to know how much new chemical will be manufactured.
Infrared spectra.-Provides a "fingerprint" for identifying the chemical.
Analytical methods.—Provides information useful for identifying the chemical.
Melting point.- Provides information about the physical state (liquid or solid) of the chemical during use.
Boiling point.-Provides information about the physical state (liquid or gas) of the chemical during use and some information about volatility.
Density.—Provides information about whether the chemical will float or sink in water.
Vapor pressure. —Provides key information about potential for exposure through inhalation and escape of the substance into the atmosphere.
Water solubility.—Provides information about chemical behavior in water and an indication of the likelihood of chemical being taken up by animals and humans.
Partition coefficient.—This measurement reflects the relative affinity of a chemical for an aqueous versus an organic environment. It is important for making predictions about a substance's persistence in various environments.
Transportation. — Information about the method(s) used to move the chemical from site to site,
Emergency Information.—Warning of possible hazards of the chemical and methods to decontaminate people and areas.

SOURCE: In part from Mazza (1982); Office of Technology Assessment.

HOW MANY PHYSICAL-CHEMICAL DATA WERE SUBMITTED ON PMNs?

Data about the nine physical-chemical items listed in table **6** are collected by companies in the development and manufacture of at least some chemicals because such information is necessary or at least highly desirable to characterize the chemical and manage its manufacture. None of the items of physical-chemical data listed in table **6** is specified in the Toxic Substances Control Act

98-826 0 - 83 - 7

(TSCA), but reporting of such data in "the possession or control" of the submitter is provided for by the general reporting requirements.

The data in table 7 show that none of the PMNs examined by OTA reported all the items of physical-chemical data listed there. Also shown is the fact that only 29 of the PMNs, 4 percent of the total, reported none of the physical-chemical items listed in the table.

There are, of course, several possible reasons for physical-chemical data not being present in the PMN. First, the submitter might not have the data because they have no value in the development or manufacture of the chemical. Second, the submitter might have some data, but, for one reason or another, not reported them. Third, data may have been lost from the file.

There was general agreement among reviewers of the first draft of this background paper that it would be unusual for a submitter to develop data about all items shown on table **6.** For instance, knowledge of the melting point is useful for a chemical that exists as a solid and a liquid under the conditions of manufacture and use; knowledge of the boiling point might be less important. Similarly, knowledge of the vapor pressure of a solid has little usefulness. Arguments like these certainly can be advanced to explain why none of the PMNs reported all the items and emphasize that submitters develop and collect data that are important to them. Since EPA is most interested in the properties of the chemicals under normal exposure conditions, the data collected by submitters should be useful to the Agency also.

One reviewer expressed the opinion that it is impossible to develop a chemical for manufacture without some physical-chemical data. The same reviewer also suggested that some submitters might elect not to report physical-chemical data because those items are not specified in TSCA.

Other reviewers emphasized that a new chemical that represents only a small change from an existing chemical may require few physical-chemical measurements to manage its development and manufacture. As an example, a reviewer suggested that a new polymer that differed from an existing polymer only in being somewhat longer might be produced without developing new physical-chemical data.

The physical-chemical datum most frequently reported was purity, followed by information about analytical methods. Those two items are especially important to the manufacturer. Knowledge of purity is necessary to any estimates of how much of the new chemical will be made, and analytical methods are necessary to locate and measure the substance.

The items that are most directly related to predicting the behavior of a chemical in the environment and its likelihood of being taken up by animals and humans—melting point, boiling point, density, volubility in water, and partition coefficient—were reported less frequently. Of these, sol-

Table 7.–Number of Physical-Chemical Data [terns Submitted on PMNs

	Manufactured		Nonmanufactured		June 1982		Regulated	Total	
	Number	Percent	Number	Percent	Number	Percent	Number	Number	Percent
PMNs	331	100	330	100	70	100	9	740	100
Infrared spectra	57	17	25	8	4	6	0	*86*	*12*
Purity	269	58	222	67	49	70	3	543	73
Analytical methods	191	58	176	53	39	56	8	414	56
Melting point	83	25	78	24	11	16	7	179	24
Boiling point	92	28	97	29	23	33	7	219	30
Density	61	18	63	19	9	13	7	140	19
Vapor pressure	83	25	73	22	18	26	6	180	24
Volubility (water)	149	45	129	39	27	39	3	308	42
Partition coefficient	15	5	11	3	0	—	1	*27*	4
Transportation	238	72	197	60	47	67	0	482	65
Emergency information	107	32	111	34	31	44	6	255	34
—all	0		0	—	o	—	o	0	—
—none	*9*	*' 3*	19	6	1	1	0	*29*	*4*

SOURCE: Office of Technology Assessment.

ubility in water was reported on 42 percent of all PMNs and melting point and boiling point on 24 and 30 percent respectively. Vapor pressure was reported on 24 percent and partition coefficient on 4 percent.

A reviewer pointed out that measurements such as melting points and boiling points are only possible on relatively pure substances. Many commercial chemicals are not so pure and such measurements, even if they were made, according to the reviewer, would be meaningless. Additionally, EPA reported that the majority of PMNs describe solid materials and that some measurements, especially vapor pressure, have little value for those substances.

The partition coefficient, which measures the relative affinity of a chemical for both aqueous and organic environments, is gaining wide acceptance as being especially useful in making predictions about possible bioaccumulation of a chemical. Its usefulness is limited to substances that are soluble in both octanol and water. Despite that limitation, EPA staff reported that partition coefficients are very important in making estimates of effects on the environment. It was often used in PMN reviews, and when it was not supplied on the PMN (it was absent from **96** percent), EPA reviewers estimated the partition coefficient based on knowledge of related chemicals.

An industry reviewer drew attention to an important piece of information that EPA often obtains on the PMN or subsequently requests. A simple "block diagram" of the process by which the chemical is to be made supplies much information about the temperatures and conditions of manufacture that is useful in assessing worker exposure and learning about the properties of the chemical. Another reviewer from an environmental organization also mentioned the block diagrams but characterized them as less valuable for risk assessment than are more detailed descriptions of the manufacturing processes. Unfortunately, OTA did not collect data about the frequency with which process descriptions were reported.

PHYSICAL-CHEMICAL DATA WERE REPORTED MORE FREQUENTLY ON MANUFACTURED PMNs

The data in table 7 show that PMNs that described manufactured chemicals were more complete in reporting physical-chemical data. An explanation for this observation could be that more data have been accumulated on chemicals that are *closer* to being manufactured. In other words, if a submitter waits to file a PMN until he is more nearly ready to produce the chemical, he may have accumulated more information about the chemical.

Table **8** reports an examination of the possibility that chemicals for which PMNs were submitted closer to the time of manufacture reported more information about physical-chemical properties of the substance. Manufactured chemicals were divided into eight groups-those for which notices of commencement of manufacture were filed before the end of the 90-day review period and those filed within 1 to **9** days, **10** to **29** days, **30** to **89** days, **90** to **119** days, 120 *to* **179** days, 180 to **365** days, and more than 1 year after the end of the review period. Inspection of table 8 does not reveal any consistent pattern in completeness of reporting and does not support the idea that the amount of physical-chemical information submitted on PMNs depends on the length of time between submission and manufacture.

The reason for more complete reporting on manufactured chemicals is not known, and further analysis would be necessary to find it. In absence of that knowledge, the apparent difference between manufactured and yet-to-be manufactured chemicals remain an interesting observation.

Table 8.—Completeness of PMNs for Physical-Chemical Information as a Function of the Time Between End of the Review Period and the Commencement of Manufacture

	Time to notice of commencement														
	<1 day	1-9 days		10-29 days		30-89 days		90-119 days		120-179 days		180-365 days		>365 days	
	No.	No.	Percent	No.	Percent	No.	Percent	No.	Percent	No.	Percent	No.	Percent	No.	Percent
PMNs	10	45	100	41	100	87	100	23	100	41	100	58	100	25	100
Infrared spectra	3	12	26	4	10	14	16	2	9	5	12	14	24	3	12
Purity	9	36	80	36	88	71	82	17	83	32	78	47	81	21	84
Analytical methods	7	30	67	20	49	55	63	9	39	22	54	34	59	13	52
Melting point	2	7	16	7	17	30	35	8	35	9	22	14	24	6	24
Boiling point	4	15	33	8	19	26	30	7	30	5	12	19	33	7	28
Density	5	11	24	7	17	15	17	4	17	3	7	9	16	6	24
Vapor pressure	5	13	29	7	17	26	30	4	17	4	10	17	29	6	24
Solubility water	4	21	47	18	44	43	49	11	48	18	44	26	45	7	28
Partition coefficient	1	1	2	0	—	3	3	0	—	2	5	7	12	1	4
Transportation	10	36	80	23	56	68	78	19	83	27	66	40	69	19	76
Emergency information	5	24	53	12	29	32	37	9	23	9	22	8	14	7	28

SOURCE: Office of Technology Assessment.

SUBMISSION OF PHYSICAL-CHEMICAL DATA ON PMNs OF DIFFERENT CLASSES

In general, less concern is attached to polymers (Class 3) substances than to other chemicals because their large size (high-molecular weight) tends to make them biologically inactive. Table 9 describes the number of polymer PMNs that contained physical-chemical data and compares that information to the same information submitted about nonpolymers (Classes 1 and 2).

As can be seen, there are few pronounced differences in reporting physical-chemical data between nonpolymers and polymers **(Class 3)** PMNs. For instance, the volubility of the chemical in water was more frequently reported for Classes 1 and 2 PMNs, probably because many polymers are water-insoluble. Although that could have been reported, it might have been left out of the submission as superfluous.

Class 2 submissions describe complex combinations of chemicals, and they less frequently report structures and formulae (see table 4) than do Class 1 submissions. However, PMNs for both Classes 1 and 2 report physical-chemical data with about the same frequencies. Therefore, despite the less frequent reporting of structure and formula for

Table 9.–Physical-Chemical Information on PMNs Describing Class 1, Class 2, and Class 3 Chemicals

	Class 1		Class 2		Class 3		Class 1 and Class 2	
	Number	Percent	Number	Percent	Number	Percent	Number	Percent
PMNs	293	100	73	100	374	100	366	100
Infrared spectra	32	11	12	16	42	11	44	12
Purity	233	80	59	81	253	67	292	80
Analytical methods	148	50	33	45	234	62	181	49
Melting point	110	36	17	23	52	14	127	35
Boiling point	69	24	31	42	119	32	100	27
Density	43	15	14	19	82	22	57	16
Vapor pressure	61	21	22	30	97	26	63	23
Volubility (water)	147	50	39	53	122	33	166	51
Partition coefficient	17	6	3	4	7	2	20	5
Transportation	155	53	45	62	283	75	200	55
Emergency information	87	30	29	40	140	37	116	32

SOURCE: Office of Technology Assessment.

Class 2 and 3 chemicals, EPA receives physical-chemical data useful for its analysis about equally for all classes of chemicals.

Transportation information was more frequently reported for polymers. The more frequent transportation information is consistent with the idea that polymers are end products of chemical production lines and moved to another manufacturing site to be incorporated into a final product. In contrast, Class 1 and 2 substances might more frequently be intermediates in production and not transported from the site of their manufacture.

The data in table 9 suggest that manufacturers develop and submit essentially the same amount of physical-chemical information about polymers and nonpolymers. At least some of the exceptions to this generalization are easily explainable given differences between the two kinds of chemicals.

SUMMARY OF FINDINGS ABOUT SUBMISSION OF PHYSICAL- CHEMICAL DATA

PMNs were inspected for the presence or absence of information about nine items concerning physical-chemical properties and whether or not emergency information and information about how the chemical was to be transported was submitted. Those items are listed and briefly described in table **6.**

None of the inspected PMNs reported all 11 items (table 7). Unlike the finding that TSCA-required information was reported equally frequently on manufactured and nonmanufactured PMNs, physical-chemical data were more frequent on manufactured PMNs.

A method was devised to investigate the possibility that manufacture of chemicals for which PMNs were prepared later in the development cycle contained more data. The idea was that a chemical that entered production very soon after submission of the PMN was further along in its development than a chemical that entered production after a longer delay. However, no consistent patterns were seen between frequencies of submission of physical-chemical data and the time between PMN submission and commencement of manufacture (table 8).

No other explanation for the dichotomy in reporting physical-chemical data on manufactured and nonmanufactured PMNs was investigated. However, there is at least one other possible explanation for the observation. Some EPA employees emphasized that the Agency does not require that the manufacturers notify the Agency of commencement of production of the chemical. Others were confident that those notices were nearly always submitted, and industry reviewers of the first draft of this report said that they understood submission of the commencement of manufacture notice was mandatory. Nevertheless, it is possible that some percentage of those PMNs listed as not manufactured do, in fact, describe chemicals that are now being produced. If that is true, the lower frequency of reporting physical-chemical data would parallel a lower frequency of notifying EPA of commencement of manufacture. This possibility was not examined, although calling submitters of nonmanufactured PMNs would be a way of exploring the possibility.

Frequency of Submission of Toxicity Information on Premanufacture Notices

6. Frequency of Submission of Toxicity Information on Premanufacture Notices

The legislative history of the Toxic Substances Control Act (TSCA) emphasizes that Congress was interested in toxic substances being identified before they enter commerce. And, of course, the most direct and immediate way of learning about toxicity is from toxicologic tests.

There are two reasons for toxicologic information appearing in a premanufacture notice (PMN) file; it could have been submitted on the original PMN, or it could have been requested by the Environmental Protection Agency (EPA). There are two avenues for request: a formal 5(e) order under TSCA, or an "informal" request with which the submitter complies.

OTA inspected each PMN for 11 items about toxicity that appear on the European Economic Community (EEC) Minimum Premarketing Data (MPD) set **(46** F.R. 8986) of required premarket testing information. Table 10 lists those items and describes their uses in risk assessment. (One toxicity item listed by EEC, a determination of any lethal effect of the substance on algal growth, was not recorded by OTA). The summary of toxicity concerns addressed in EPA's initial review of PMNs (app. A) lists many of the specific tests scored by OTA. When a test result was not reported, and that test was of importance to EPA's risk assessment, EPA scientists would have had to estimate the chemical's toxic effects based on Structural Activity Relationship (SAR) analysis.

The first three items listed on table **10,** acute toxicity tests, are similar in that they measure the lethality of the substance in laboratory animals; they differ in routes of exposure. Contact irritations and sensitizations, whether of the eye or the skin, are common problems in the workplace and in consumer uses. The two skin tests and one eye test provide estimates of the effects from short-term exposures of those organs. Repeated dose toxicity tests employ repeated doses at a level not known to cause death and measure the effects on organ systems.

Mutagenicity is the capacity to cause changes in the genetic material, DNA. Most tests for mutagenicity are "short-term" or "in vitro tests," which require a few days to a few weeks for execution and measure interactions between the chemical and DNA (11). Table 11 is a description of eight general types of short-term tests useful for measuring mutagenicity or other interactions with DNA.

Table 10.—Items of Toxicity Information That Were Scored on PMNs

Item/Usefulness in determining possible risks of chemicals
Acute oral **toxicity.—Provides information from animal tests about possible lethal or other serious effects from short-term ingestion.**
Acute dermal toxicity. **—Provides information from animal tests about possible lethal or other serious effects from short-term exposures on the skin.**
Acute inhalation **toxicity.— Provides information from animal tests about possible lethal or other serious effects of short-term inhalation.**
Skin **irritation-Provides information from animal tests about possible irritation resulting from contact with the skin.**
Skin **sensitization.—Provides information from animal tests about possible changes in the skin resulting in increased sensitivity to other substances.**
Eye irritation. **—Provides information from animal tests about possible adverse effects from the substance reaching the eye.**
Repeated dose **toxicity.—Provides information from animal tests about effects of repeated exposures on major organ systems.**
Mutagenicity.– **Provides information from tests on microorganisms, animals, or cells from various organisms about the possible mutagenicity of the chemical.**
Fish toxicity.—Provides information about possible adverse effects on fish.
Daphnia toxicity.— **Provides information about possible adverse effects on invertebrates.**
Biological accumulation/degradation. **—Provides information about the tendency of the chemical to be accumulated or to be degraded in biological systems.**
Miscellaneous.—Some PMNs included additional information from other toxicity tests and other sources.

SOURCE: In part from Mazza (1982); OTA (1981); Office of Technology Assessment.

Table 11.—Eight General Classes of Short-Term Tests That Measure Mutagenicity or Other interactions With DNA

1. Mutagenesis in bacteria and bacterial viruses.
2. Mutagenesis in yeast.
3. Mutagenesis in cultured (laboratory-grown) mammalian cells.
4. Mutagenesis affecting mouse hair color.
5. Mutagenesis in fruit fries *(Drosophila* melanogaster).
6. Effects on chromosomal mechanics in intact mammals and in mammalian cells in culture.
7. Disruption of DNA synthesis and DNA repair mechanisms in bacteria and other organisms.
8. in vitro transformation of cultured cells.

SOURCE: Off Ice of Technology Assessment (1981).

TSCA focused attention on three kinds of toxicities-carcinogenicity (the capacity to cause cancer), mutagenicity, and teratogenicity (the capacity to cause birth defects). Such "chronic toxic effects" can result from low dose exposures. Mutagenicity (certainly), carcinogenicity (generally), and teratogenicity (perhaps) result from interactions between environmental agents and DNA. Of the toxicity tests listed in table 10, only mutagenicity tests measure interactions with DNA and bear directly on questions of chronic toxic effects. Other tests for chronic toxic effects, involving large numbers of experimental animals, long periods of time, and high costs (9) are considered too expensive for new chemicals.

Fish and daphnia toxicity tests provide information about "ecotoxicity." They are especially useful in making projections about the effect of the chemical on aquatic organisms.

Biological accumulation and degradation tests provide important information about the persistence of the chemical in organisms and biological methods for degradation. The value of these tests is greatest for substances to be discharged into water, and industry reviewers of the first draft of this report pointed out that such tests are not necessary on substances that will not reach a water source. OTA did not collect information about whether or not it was planned to discharge chemicals described on PMNs into water, and so cannot comment on the appropriateness of ecotoxicity data submission.

HOW MANY TOXICOLOGIC DATA WERE SUBMITTED ON PMNs?

The number of PMNs containing toxicity information is shown on table 12. Overall, 53 percent of all PMNs inspected had some information about toxicity. PMNs that described manufactured chemicals had such information somewhat more frequently; 59 percent reported some toxicologic information. As a group, the June 1982 PMNs reported toxicity data less frequently than

Table 12.-Number of Toxicologic items Submitted on PMNs

	Manufactured		Non-manufactured		June 1982		Regulated	Total	
	No.	Percent	No.	Percent	No,	Percent	No.	No.	Percent
PMNs	331	100	330	100	70	100	9	740	100
Acute oral toxicity	165	50	126	38	25	36	1	317	43
Acute dermal toxicity	132	40	75	23	13	19	0	220	30
Acute inhalation toxicity	33	10	28	8	4	6	0	65	9
Skin irritation	124	37	101	31	21	30	1	247	33
Skin sensitization	40	12	23	7	3	4	0	66	9
Eye irritation	137	41	115	35	20	29	1	273	37
Repeated dose toxicity	56	17	28	8	0	—	1	85	11
Mutagenicity	58	18	55	17	11	16	2	126	17
Fish toxicity	35	11	26	8	1	1	2	64	9
Daphnia toxicity	16	5	12	4	1	1	0	29	4
Biological accumulation or biological degradation	20	6	12	4	4	6	0	36	5
No toxicity information	137	41	167	50	37	53	6	347	47

SOURCE: Office of Technology Assessment.

did the manufactured or nonmanufactured PMNs.

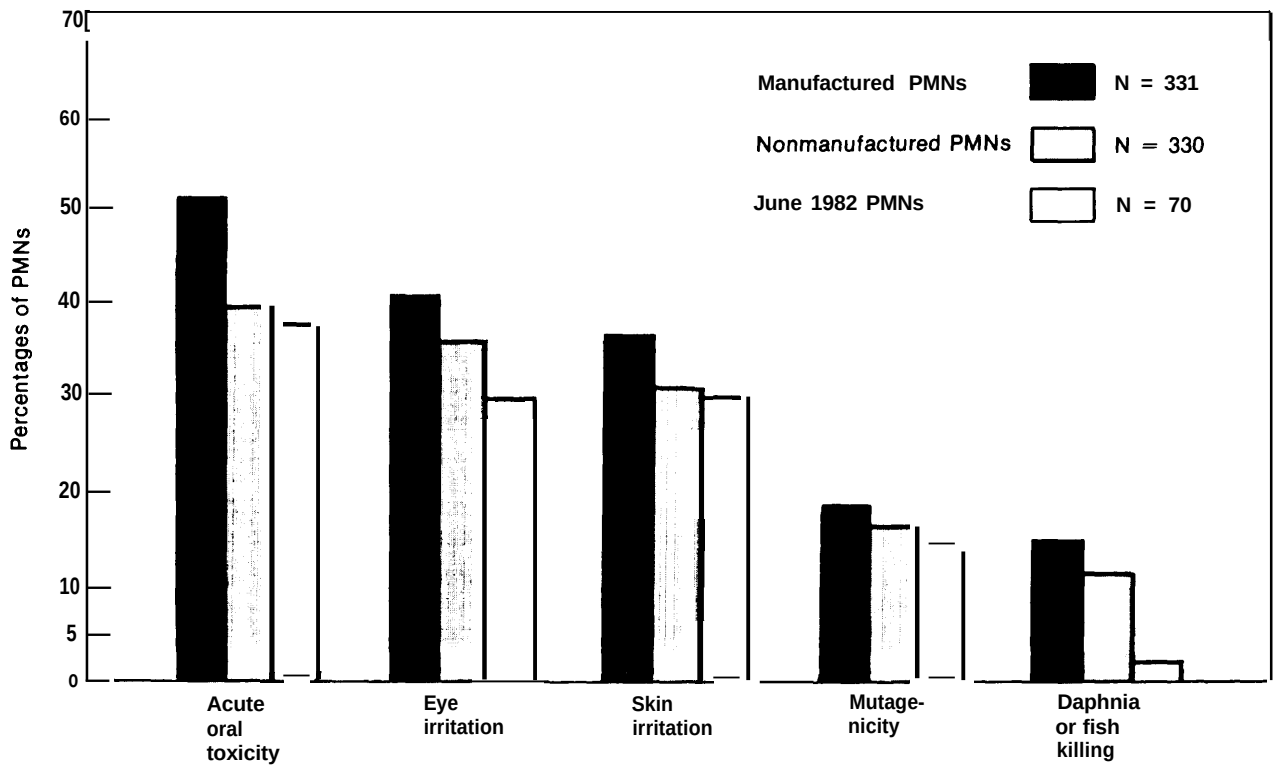
The most frequently reported toxicity tests were acute oral toxicity tests that establish the lethality of the chemical when ingested by test animals. Fifty percent of the manufactured PMN chemicals and **43** percent of all PMNs contained that kind of information. The second most frequently reported test was for eye irritation, followed closely by tests for acute dermal toxicity and skin irritations.

Mutagenicity tests, the only tests that bear on chronic toxicity, were reported on less than one-fifth (17 percent) of all PMNs. Data about ecotoxicity were reported even less frequently: fish toxicity on 9 percent of PMNs; daphnia toxicity on 4 percent; biological accumulation or degradation on 5 percent. Figure 5 is a comparison of the frequency of submission of the three most commonly reported toxicity tests and mutagenicity tests on manufactured, nonmanufactured, and June 1982 PMNs.

TSCA is written to protect against unreasonable risks to human health or the environment, and PMNs contain limited data for EPA to consider in making decisions about potential chronic toxicities or ecological toxicity. Several reviewers of the first draft of this background paper pointed to the absence of such data as a major concern. EPA can use SAR analysis to make estimates of toxicity when data are not available, but whether EPA appropriately decides that SAR analysis is sufficient can be questioned. At a more fundamental level, given the limited experience with SAR, the appropriateness of the technique can also be questioned. Unquestionably, however, it is employed.

The reduced toxicity submissions in June **1982** may be only a "blip," an abnormally low month, or it may reflect a downward trend over the peri-

Figure 5.—Percentage of PMNs Containing the Three Most Commonly Reported Toxicity Tests and the Two Tests Related to Chronic Toxicity and Ecotoxicity



SOURCE: Office of Technology Assessment.

od June 1981 to June 1982. The observed drop in reporting of all toxicity information items was not paralleled by a drop in physical-chemical data reporting. June 1982 PMNs were highest in the frequency with which 4 of the 11 physical-chemical items were reported (see table 7).

A number of reviewers objected to drawing even a tentative conclusion from comparing the June **1982** data to earlier data. One group of industry reviewers inspected the publicly available records for the June **1982** PMNs and provided its appraisal of those for which no toxicity information was reported. According to the opinions of those industry reviewers, the June **1982** PMNs that contained no toxicity data described chemicals that were not hazardous.

Another reviewer (not from an environmental group), drew a very different conclusion from the comparison of June **1982** data to earlier data. In his opinion, if the decrease in toxicity data reporting is general and not confined to the single month of June 1982, it reflects an industry perception that EPA is no longer so serious about PMN reporting. In turn, that perception of decreased EPA concern about new chemicals is being translated into reduced industry attention being paid to learning about potential toxicity.

TOXICITY DATA WERE MORE FREQUENTLY REPORTED ON MANUFACTURED PMNs

Just as was found for physical-chemical data, PMNs describing now-manufactured chemicals contain more toxicity information than PMNs for substances not yet manufactured. The same sort of analysis described in table 8 was applied to toxicity data. As is shown on table 13, there is no consistent relationship between time required for commencement of manufacture and amount of submitted toxicity information. Therefore, although more toxicity and physical chemical data are reported for manufactured PMNs, the completeness of reporting does not appear to be a function of how close to manufacture the substance was when the PMN was submitted. Instead, these observations may suggest that submitters' analyses permit them to judge accurately which substances are more likely to be manufactured and to produce more information about them.

Table 13.—Completeness of PMNs for Toxicity Information as a Function of the Time Between End of the Review Period and the Commencement of Manufacture

	Time to notice of commencement													
	<1 day	1-9 days		10-29 days		30-89 days		90-119 days		120-179 days		160-365 days		>365 days	
	No.	No.	Percent	No.	Percent	No.	Percent	No.	Percent	No.	Percent	No.	Percent	No.	Percent
PMNs	10	45	100	41	100	87	100	23	100	41	100	58	100	25	100
Acute oral toxicity	3	29	44	17	41	50	57	10	43	20	99	26	45	19	76
Acute dermal toxicity	3	19	42	12	29	38	44	10	43	13	30	24	41	13	42
Acute inhalation toxicity	0	5	11	7	17	10	11	1	4	3	7	4	7	3	12
Skin irritation	3	14	31	13	32	36	41	9	39	13	30	23	40	13	42
Skin sensitization	0	4	8	7	17	7	8	6	26	4	10	8	14	4	12
Eye irritation	2	18	40	14	34	42	48	8	35	14	34	23	40	16	48
Repeated dose toxicity	0	3	6	5	12	12	14	5	22	8	20	12	21	11	44
Mutagenicity	1	3	6	7	17	15	17	5	22	4	10	19	33	4	16
Fish toxicity	1	4	8	3	7	9	10	4	17	3	7	7	12	4	16
Daphnia toxicity	1	0	–	2	5	2	2	3	13	1	2	4	7	3	12
Biological accumulation or biological degradation	0	3	6	1	2	7	8	0	–	4	10	3	5	2	8

SOURCE: Office of Technology Assessment.

SUBMISSION OF TOXICITY DATA ON PMNs DESCRIBING DIFFERENT CLASSES OF CHEMICALS

As a class, polymers are associated with less hazard than some other chemicals, and some substances of this class are being proposed for exemption from PMN review by EPA (see table 2). In many cases, the large size (high-molecular weight) of polymers makes them biologically inactive because they cannot be taken up by most cells. For that reason, EPA considers toxicity information to be of less importance for Class 3 chemicals (polymers) and of more importance for the Class 1 and 2 chemicals.

Table 14 shows the frequency, by class of chemical, with which toxicologic information was submitted on PMNs, and figure **6** shows the frequency of submission of the three most common toxicity items and mutagenicity and ecotoxicity. In keeping with the inherently lower toxicity of polymers, less testing was reported for those substances.

More importantly, perhaps, removing Class 3 chemicals, polymers, from consideration allows computation of the frequency with which toxicity data for Classes 1 and 2 are submitted. Sixty-one percent of nonpolymer PMNs reported acute oral toxicity data, eye irritation was reported on **52** percent, and skin irritation on 49 percent. Mutagenicity data, important to making estimates of chronic toxicity, were submitted on 27 percent of Classes 1 and 2 PMNs and fish toxicity and daphnia toxicity on 13 and 5 percent respectively (table 14).

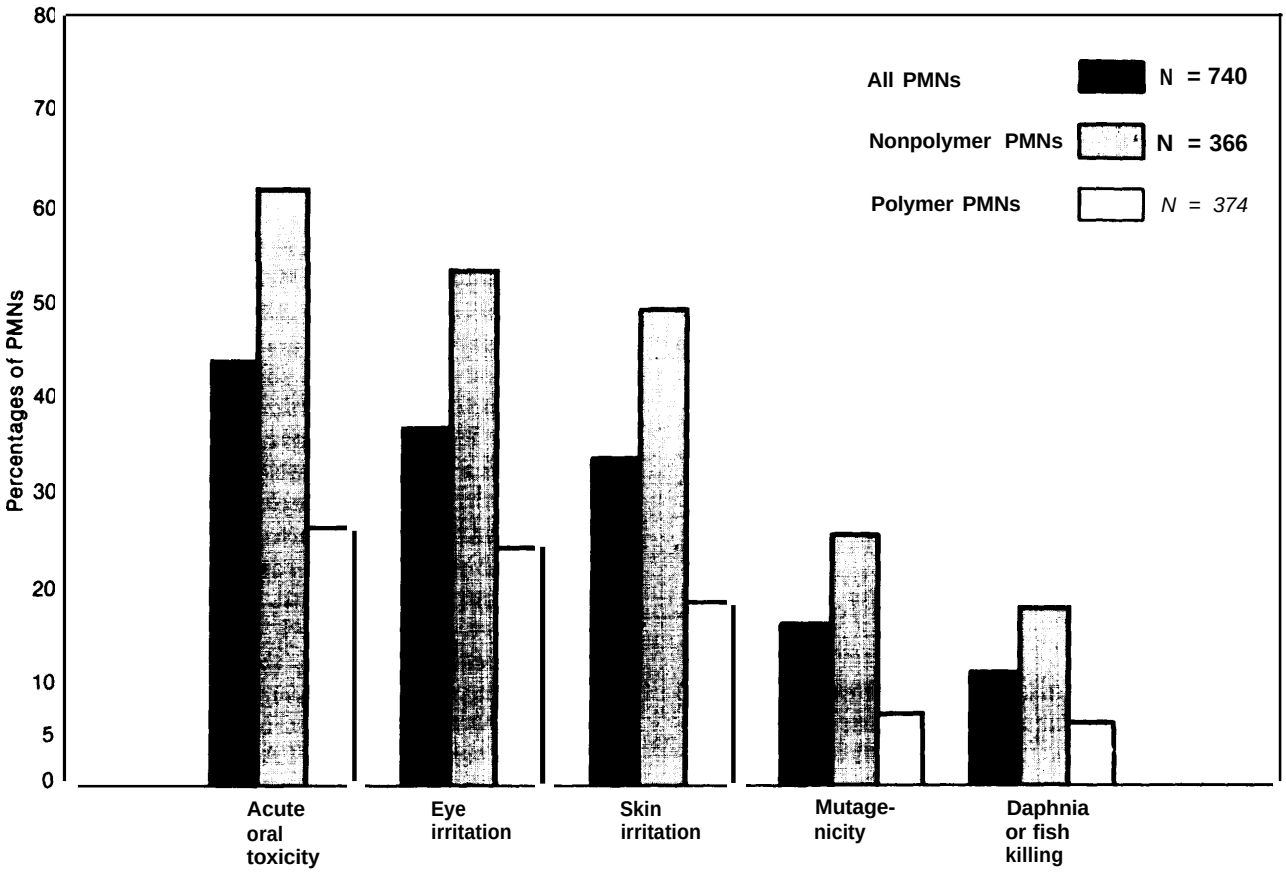
If the proposition is accepted that toxicity data are less likely to be needed for evaluating polymer PMNs, the data in table 14 can be taken, with some caveats, as a more accurate representation of frequency of toxicity submission. However, some monomers from which polymers are made are toxic. If a polymer preparation is contaminated with a significant fraction of free monomers or low-molecular weight polymers, toxicity information would be important. Polymer PMNs sometimes report the percentage of monomers present, but OTA did not attempt to correlate percentages of monomeric and low-molecular weight contamination with submitted toxicity data. By the same token, some of the Class 3 polymers PMNs that submitted toxicity data reported monomer toxicity, but OTA did not record those details. In addition, reviewers of the first draft of this report drew attention to the possible contamination of polymers with catalysts and other chemicals used in their manufacture.

Table 14.—Toxicity Information on PMNs Describing Class 1, Class 2, and Class 3 Chemicals

	Class 1		Class 2		Class 3		Class 1 and Class 2	
	No.	Percent	No.	Percent	No.	Percent	No.	Percent
PMNs	293	100	73	100	374	100	366	100
Acute oral toxicity	178	61	44	60	96	26	222	61
Acute dermal toxicity	120	41	33	45	68	18	153	42
Acute inhalation toxicity	34	12	8	11	24	5	42	11
Skin irritation	147	50	32	44	69	18	179	49
Skin sensitization	42	14	8	11	16	4	5 0	14
Eye irritation	153	52	36	49	85	23	189	52
Repeated dose toxicity	52	18	10	14	24	6	62	17
Mutagenicity	82	28	16	22	28	7	98	27
Fish toxicity	43	15	5	7	16	4	48	13
Daphnia toxicity	20	7	0	–	9	2	20	5
Biological accumulation or biological degradation	25	9	4	5	7	2	29	8

SOURCE: Office of Technology Assessment.

Figure 6.-Percentage of Polymer and Nonpolymer PMNs That Contained the Three Most Commonly Reported-Toxicity-Tests and Tests Related to Chronic Toxicity and Ecotoxicity



SOURCE: Office of Technology Assessment.

Submission of Physical-Chemical and Toxicity Information on Some Subgroups of Premanufacture Notices

7

Submission of Physical= Chemical and Toxicity Information on Some Subgroups of Premanufacture Notices

PMNs SUBMITTED FOR CONSUMER PRODUCTS

Risk assessment encompasses two elements: 1) estimates of *hazard,* a property that resides in an object or substance or behavior; and 2) exposure that depends on estimates of the number of people or organisms that may come in contact with various amounts of the hazard for various times through different media. The highest exposure, in terms of people likely to be exposed, are associated with products intended for consumer use. Therefore, knowledge of hazard is especially important for these items.

Not only are there many consumers, but the chances for misuse probably increase with the number of users. Consumer-use items are purchased in retail outlets and may or may not be used according to directions. Labels and instructions may be lost, washed off, ignored, or not understood. A particularly striking example of such an occurrence was the mistaken use of a lemon-scented dishwashing detergent to flavor tea when samples of the product were mailed to consumers in 1982.

Table 15 presents the frequency with which physical-chemical and toxicologic data were submitted for consumer-use premanufacture notices (PMNs) and all other PMNs, and figure 7 shows the frequency of submission of some toxicity data. There were only small differences in the frequency of submission of physical-chemical data. Nine of the eleven toxicologic data were more frequently reported on consumer products. The two exceptions are reporting of acute inhalation toxicity and mutagenicity.

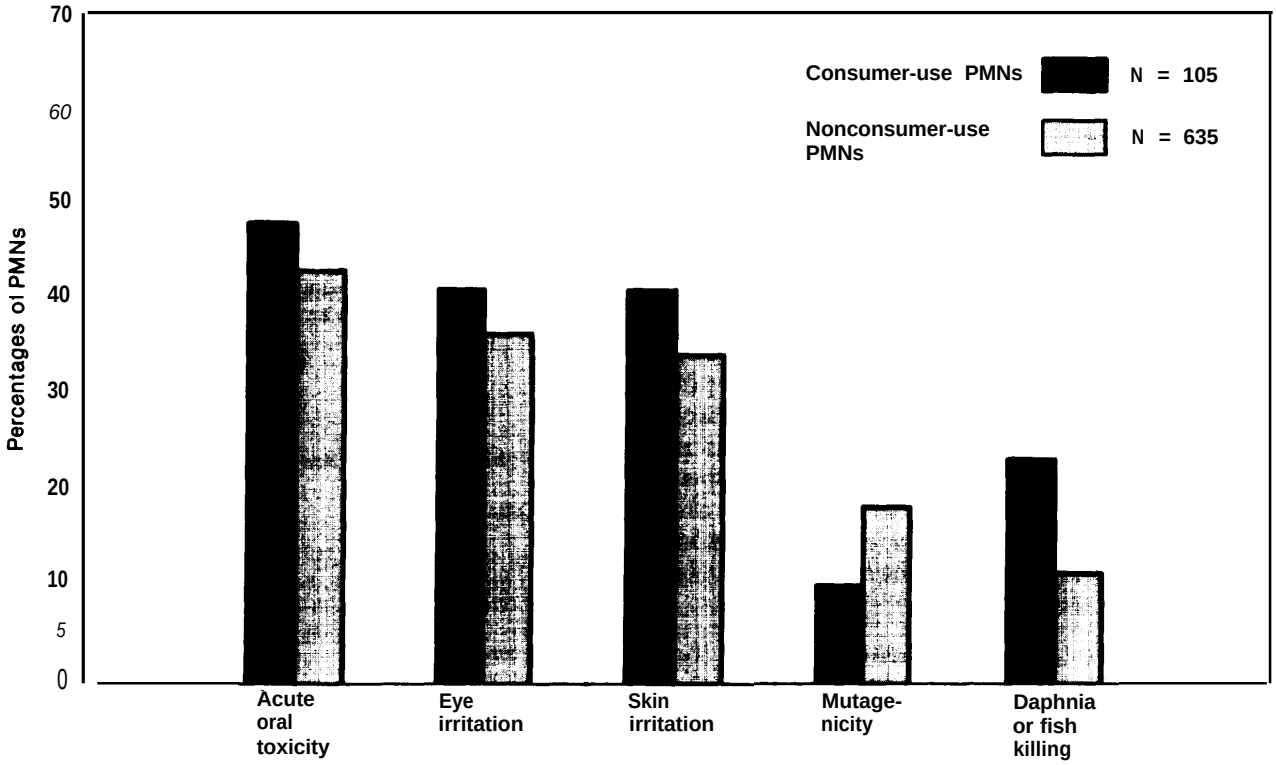
The overall more frequent submission of toxicity data fits with the idea that greater concern is frequently attached to consumer-use products. Because of the potentially great number of people exposed to these products, more information about any hazard is desirable to make reasonable decisions about risk. Despite the more frequent reporting of toxicity information on the consumer-use PMNs, more than half of such PMNs reported no toxicity data (see tables 18, 19, and 20).

Table 15.—Completeness of PMNs Submitted for Consumer-Use Products as Compared to Other PMNs

	Consumer-use PMNs		All other PMNs	
	No.	Percent	No.	Percent
Physical-chemical Information:				
PMNs	105	100	635	100
Infrared spectra	18	17	68	11
Purity	71	68	472	74
Analytical methods	63	60	351	55
Melting point	23	22	156	25
Boiling point	25	24	194	31
Density	22	21	118	19
Vapor pressure	27	26	153	24
Volubility water	45	42	263	41
Partition coefficient	4	4	23	4
Transportation	79	75	403	63
Emergency information	31	30	224	35
Toxicology information:				
Acute oral toxicity	50	48	270	43
Acute dermal toxicity	39	37	183	30
Acute inhalation toxicity	6	6	61	10
Skin irritation	39	48	211	33
Skin sensitization	17	16	49	8
Eye irritation	44	42	232	37
Repeated dose toxicity	20	19	66	10
Mutagenicity	11	10	116	18
Fish toxicity	14	13	50	8
Daphnia toxicity	10	10	19	3
Biological accumulation or biological degradation	5	5	31	5

SOURCE: Office of Technology Assessment.

Figure 7.-Percentage of PMNs That Described Consumer-Use or Nonconsumer-Use Products and Contained the Three Most Commonly Reported Toxicity Tests and Tests Related to Chronic Toxicity and Ecotoxicity



SOURCE: Office of Technology Assessment.

PMNs SUBMITTED FOR POLYMERS

According to the Environmental Protection Agency's (EPA) proposed exemption of polymers from PMN reporting requirements, polymers' high molecular weights make them inactive in most biological systems, and that property alone is sufficient to reduce the need for information about toxicity. OTA's findings about the amounts of information on polymer PMNs is presented in tables 9 and 14. Consistent with the idea that polymers were less hazardous, toxicity data were less frequently reported for those substances (table 14). The observation that physical-chemical data items were reported about equally for both polymers and non-polymers reflects the usefulness or necessity of such data in describing and identifying a chemical in the manufacturing plant.

EPA now receives fewer toxicity data about polymers than other substances. The proposed polymer exemption policy is expected to reduce further the amount of toxicity data submitted about those chemicals, but the tendency toward less information is already established. An interesting question that could be addressed by examining polymer PMNs in detail is whether or not toxicity information was more often submitted on PMNs that describe substances to be excluded from the exemption (see table 2).

PMNs SUBMITTED FOR SITE= LIMITED CHEMICALS

The number of people exposed to site-limited intermediates is necessarily limited. EPA's proposed exemption of these substances is based on the idea that knowledge about the use of these chemicals at their site of manufacture will be sufficient to make a decision between whether they may or may not present an unreasonable risk. Although the number of people that might be exposed is limited to those at the production site, exposure levels are potentially quite high. There may be a special incentive for companies to test site-limited intermediates because of concern about high-exposure levels.

OTA used the information provided on the PMNs to sort out the notices that described site-limited chemicals (see table 16). The notices examined by OTA are not exactly comparable to the group of chemicals proposed for exemption. EPA proposes to exempt site-limited intermediates, which are consumed or otherwise used only at the site of manufacture. OTA examined a somewhat larger universe, all those PMNs that described site-limited chemicals. The distinction between the two categories "site-limited intermediates" and "site-limited chemicals" is not entirely clear, but the first category is part of the second.

Table 16 shows a comparison of the amounts of physical-chemical information and toxicity data submitted for site-limited chemicals and all other chemicals. Overall, physical-chemical information was reported about equally on both groups of PMNs, and toxicity information was reported more frequently for site-limited chemicals. Over half (52 percent) of the PMNs describing site-limited chemicals reported oral toxicity data; 42 percent of the others did.

The equal reporting of physical-chemical information is to be expected. In general, such information is necessary for the manufacturer regardless of whether or not the chemical is moved from site to site. One item that is submitted less frequently on site-limited PMNs is information about transportation, which is completely reasonable for such chemicals.

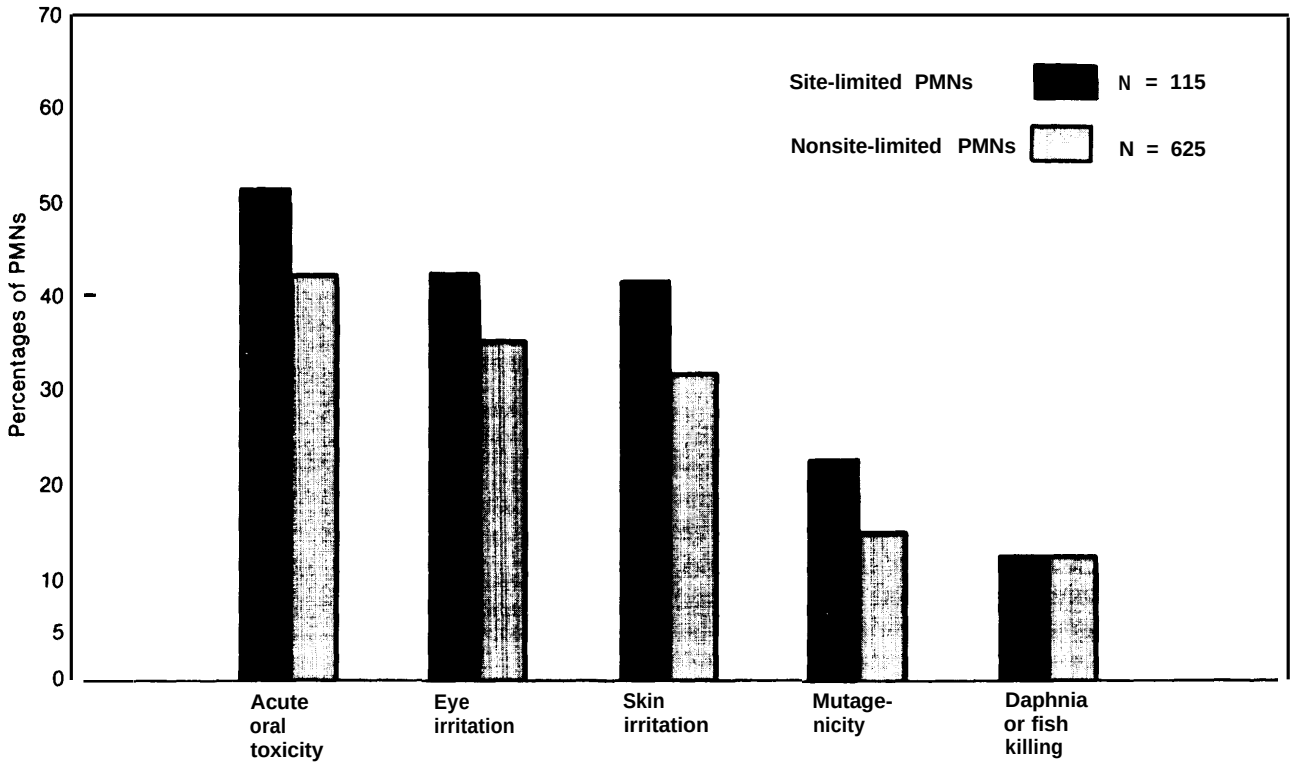
As shown on table **16** and figure **8,** toxicity information was reported more frequently for site-limited chemicals than for all others. Since EPA cannot require testing of new chemicals simply because they are new, it can be assumed that the development of toxicity information is done by manufacturers for their own needs.

Table 16.—Physical-Chemical and Toxicity information Submitted for Site-Limited Chemical PMNs and All Other PMNs

	Site- limited chemical PMNs		All other PMNs	
	No.	Percent	No.	Percent
Physical-chemical Information:				
PMNs	115	100	625	100
Infrared spectra	17	15	69	11
Purity	89	77	454	73
Analytical methods	68	59	346	55
Melting point	31	27	148	24
Boiling point	19	17	200	32
Density	14	12	126	20
Vapor pressure	21	18	159	25
Volubility water	51	44	259	41
Partition coefficient	1	<1	26	4
Transportation	49	43	433	69
Emergency information	30	26	225	36
Toxicology Information:				
Acute oral toxicity	60	52	260	42
Acute dermal toxicity	46	40	76	12
Acute inhalation toxicity	11	10	55	9
Skin irritation	50	43	200	32
Skin sensitization	16	14	50	8
Eye irritation	48	42	228	36
Repeated dose toxicity	14	12	72	12
Mutagenicity	25	22	102	16
Fish toxicity	12	10	52	8
Daphnia toxicity	2	2	27	4
Biological accumulation or biological degradation	6	5	30	5

SOURCE: Off Ice of Technology Assessment.

Figure 8.-Percentage of PMNs That Described Site= Limited or Other Chemicals and Contained the Three Most Commonly-Reported Toxicity Tests and Tests Related to Chronic Toxicity and Ecotoxicity



SOURCE: Office of Technology Assessment.

PMNs SUBMITTED FOR LOW-PRODUCTION-VOLUME CHEMICALS

The proposed low-volume exemptions argue that limited production volumes reduce the amount of information that EPA requires to make a judgment about any unreasonable risk that may be associated with a new chemical. An important caveat to any such generalization is that toxicity varies over an extremely wide range, and a miniscule amount of a very potent toxic substance can cause illness and death. However, most substances are not extremely toxic, and, regardless of toxicity, reduced exposure limits risk.

In general, substances to be manufactured in quantities less than 10,000 kg per year will be exempted from the usual PMN review unless they may cause serious acute or chronic health effects or significant environmental effects under conditions of use. The exemptions are discussed in ch. 2.

Some reviewers of the first draft of this report commented that EPA had truncated the review of some low-volume PMNs in the past. The shortened reviews were reported to have depended on professional judgment that: 1) production volumes were limited, and 2) either potential toxicity or exposure or both was low. Those reviewers characterized the proposed low-volume exemptions as being an extreme position because they depend so heavily on predicted production volumes.

For both low production volume exemptions, EPA will inspect the notice to assure that the

chemical qualifies for exemption. No chemical that receives a low-volume exemption will go on the Inventory. Therefore, manufacture of those substances by other companies will only be possible after submission of a PMN by the second company.

When (or if) the production volume exceeds **10,000** kg per year, EPA intends to require that the manufacturer submit a PMN for the substance. When PMN review is complete, the chemical will go on the Inventory. Part of the rationale for the low-volume exemption is that manufacturers will be better able to bear the reporting costs of the PMN review as production volume increases.

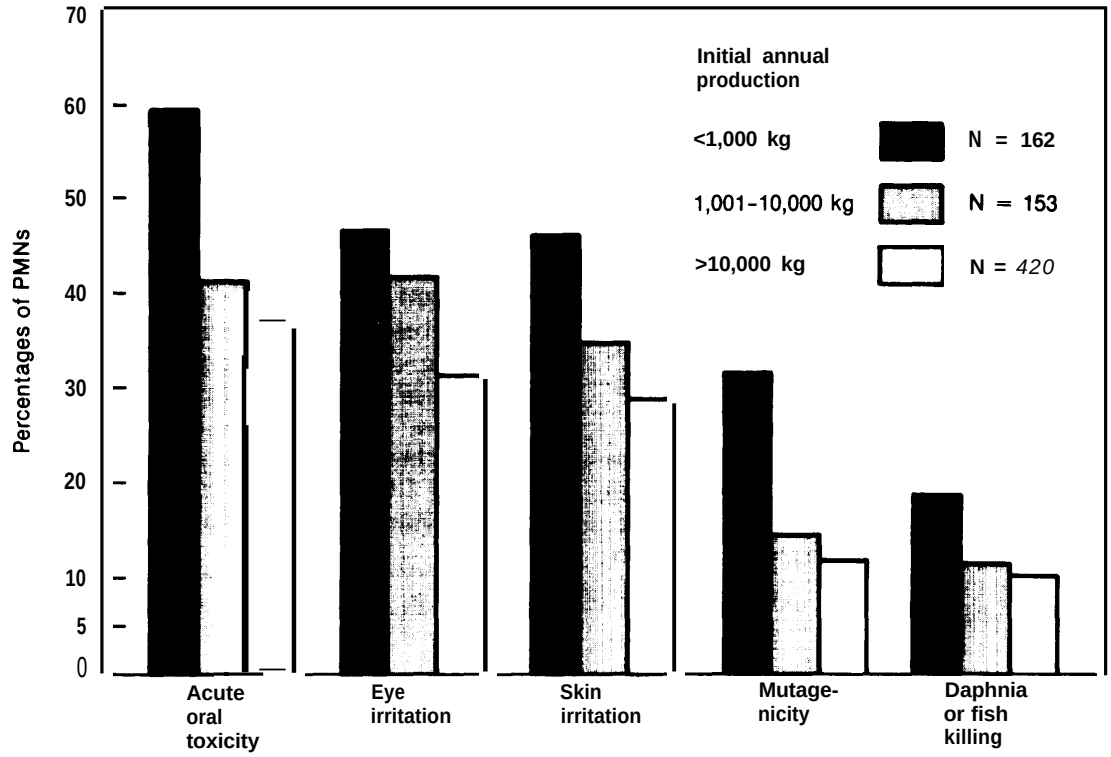
Table 17 reports and figure 9 abstracts some of the information content of PMNs reviewed for chemicals to be made in quantities of **1,000** kg or less in the first year, those to be made in quantities of 1,000 to 10,000 kg in the first year and all others. The frequency with which physical-chemical data are submitted fluctuates among the three volume classes, but there appears to have been more frequent reporting of toxicity information for PMNs that describe low-volume chemicals. The most striking differences in frequency of reporting toxicity data are acute ingestion toxicity and mutagenicity. Data from acute ingestion toxicity studies were reported on 59 percent of chemicals slated for production in volumes less than 1,000 kg; on 41 percent of those to be manufactured in volumes between **1,001** and 10,000 kg; and on 37 percent of those to be made in volumes greater than 10,000 kg. Mutagenicity data were reported more often for the lower volume chemicals; 31, 14, and 12 percent for the less than 1,000, between 1,001 and 10,000, and greater than 10,000 kg classes respectively.

Table 17.—Physical-Chemical and Toxicity Information Submitted on PMNs That Project Initial Year Production Volumes of 1,000 Kilograms or less, of Between 1,001 and 10,000 Kilograms, and All Others

	Initial year production volume					
	<1,000 kg		1,001-10,000 kg		>10,000 kg	
	No.	Percent	No.	Percent	No.	Percent
Physical-chemical Information:						
PMNs	162	100	153	100	420	100
Infrared spectra	14	8	19	12	53	13
Purity	118	73	117	76	305	73
Analytical methods	73	45	87	57	254	60
Melting point	61	38	34	22	83	20
Boiling point	38	23	39	25	141	34
Density	19	12	20	13	98	23
Vapor pressure	36	22	22	14	122	29
Volubility water	73	45	63	41	169	40
Partition coefficient	4	2	4	3	19	4
Transportation	84	52	99	65	297	71
Emergency information	47	29	60	39	148	35
Toxicology information:						
Acute oral toxicity	98	59	64	41	154	37
Acute dermal toxicity	51	31	44	29	124	30
Acute inhalation toxicity	11	7	17	11	38	9
Skin irritation	74	47	53	35	118	28
Skin sensitization	25	15	12	8	29	7
Eye irritation	76	47	66	43	136	32
Repeated dose toxicity	29	18	14	9	41	10
Mutagenicity	51	31	22	14	52	12
Fish toxicity	19	12	13	8	32	8
Daphnia toxicity	10	6	6	4	13	3
Biological accumulation or biological degradation	9	5	6	4	21	5

SOURCE: Office of Technology Assessment.

Figure 9.—Percentage of PMNs That Described Low- or High-Production-Volume Chemicals and Contained the Three Most Commonly Reported Toxicity Tests and Tests Related to Chronic Toxicity and Ecotoxicity



SOURCE: Office of Technology Assessment.

COMPARISON OF TOXICITY DATA SUBMITTED ON CONSUMER AND NONCONSUMER SUBSTANCES, BOTH POLYMERS AND NONPOLYMERS, SCHEDULED FOR PRODUCTION IN DIFFERENT AMOUNTS

The finding that PMNs that described low-volume chemicals reported toxicity data more frequently might reflect a reluctance on the part of manufacturers to test high-volume chemicals or to report results. Given that the risk estimate for high-volume chemicals is already elevated because of high potential exposure, manufacturers might think that any hint of toxicity may cause EPA to require even more testing to allay fears. Furthermore a company that submits a PMN expects to manufacture the chemical, and it is not interested in expending more time and energy on additional tests. Therefore there might be few incentives for a company to test or to report test results on high-volume chemicals.

Alternatively, OTA considered that fewer toxicity data are reported for high-volume chemicals because manufacturers have had a great deal of experience with closely related substances and are satisfied that the new chemicals are not hazardous. An obvious class of such chemicals is polymers.

The data presented in table 18 show the frequency of submission of toxicity data for polymers and nonpolymers at different projected pro-

Table 18.—Number of Submissions of Toxicity Data on Polymers and Nonpolymers To Be Produced in Different Amounts

	<1,000 kg				1,001-10,000 kg				>10,000 kg			
	Polymer		Non polymer		Polymer		Non polymer		Polymer		Non polymer	
	No.	Percent	No.	Percent	No.	Percent	No.	Percent	No.	Percent	No.	Percent
PMNs	37	100	127	100	56	100	100	100	291	100	143	100
Acute oral toxicity	16	43	80	63	14	25	50	50	65	22	89	62
Acute dermal toxicity	6	16	45	35	8	14	36	36	53	18	71	50
Acute inhalation toxicity	1	2	10	8	6	11	11	11	17	6	21	15
Skin irritation	11	30	63	50	16	29	37	37	42	14	76	53
Skin sensitization	1	1	24	19	6	11	6	6	9	3	20	14
Eye irritation	13	35	63	50	18	32	43	43	54	19	82	57
Repeated dose toxicity	4	11	25	*20*	*4*	*7*	10	10	15	5	26	18
Mutagenicity	8	*22*	*43*	*34*	1	2	21	21	*19*	*7*	*33*	*23*
Fish toxicity	4	11	15	12	2	4	11	11	10	3	22	15
Daphnia toxicity	2	5	8	6	1	2	5	5	6	2	7	5
Biological accumulation or biological degradation	0	—	9	7	0	–	6	6	7	2	14	10

SOURCE: Office of Technology Assessment.

duction volumes. As can be seen, fewer data were submitted on polymers at all production volumes. For nonpolymers, toxicity data submission was more frequent on the PMNs that predicted higher production volumes.

The data relating polymers and production volumes were further broken down to examine submission of toxicity data on consumer products (tables **19** and **20).** Toxicity data were more frequently submitted on nonpolymers whether they described consumer- or nonconsumer-use chemicals. For nonpolymers to be made in greater than 10,000 kg volumes annually, the reporting of toxicity data was more frequent than for PMNs as a whole (compare table 12 with tables 19 and **20).** The frequency of submission of toxicity data for nonpolymers was generally higher for substances intended for consumer use (tables 19 and 20).

Another observation to be made from table 19 is that over half **(56** percent) of consumer-use PMNs described chemicals to be made in volumes greater than 10,000 kg annually. Therefore, less than half (44 percent) of consumer-use chemicals, which are of special concern because of their exposure characteristics, were slated for production

Table 19.-Number of Submissions of Toxicity Data on PMNs Describing Consumer-Use Chemicals and Polymers and Nonpolymers To Be Produced in Different Amounts

	<1,000 kg		1,001-10,000 kg		>10,000 kg			
					Polymer		Nonpolymer	
	No. polymer	No. nonpolymer	No. polymer	No. nonpolymer	No.	Percent	No.	Percent
PMNs	2	19	10	15	35	100	23	100
Acute oral toxicity	1	11	2	7	12	34	16	70
Acute dermal toxicity	1	7	1	6	12	34	12	52
Acute inhalation toxicity	0	0	0	1	2	6	3	13
Skin irritation	1	9	2	6	7	21	13	57
Skin sensitization	0	6	1	3	3	9	4	17
Eye irritation	1	7	2	6	13	38	15	65
Repeated dose toxicity	0	5	1	1	4	12	8	35
Mutagenicity	0	3	0	0	4	12	4	17
Fish toxicity	1	2	1	1	3	9	6	26
Daphnia toxicity	1	2	0	1	3	9	3	13
Biological accumulation or biological degradation	0	0	0	1	1	3	3	13

SOURCE: Office of Technology Assessment.

Table 20.—Number of Submissions of Toxicity Data on PMNs Describing Nonconsumer-Use Chemicals and Polymers and Nonpolymers To Be Produced in Different Amounts

	<1,000 kg				1,001-10,000 kg				>10,000 kg			
	Polymer		Non polymer		Polymer		Non polymer		Polymer		Nonpolymer	
	No.	Percent	No.	Percent	No.	Percent	No.	Percent	No.	Percent	No,	Percent
PMNs	35	100	108	100	46	100	85	100	256	100	120	100
Acute oral toxicity	15	43	70	65	12	26	43	51	53	21	74	62
Acute dermal toxicity	5	14	38	35	7	15	30	35	41	16	60	50
Acute inhalation toxicity	1	3	10	9	6	13	10	12	15	6	19	11
Skin irritation	10	29	55	51	14	30	31	36	35	14	64	53
Skin sensitization	1	3	18	17	5	11	3	4	6	2	16	13
Eye irritation	12	34	57	53	16	35	37	44	41	16	68	57
Repeated dose toxicity	4	11	20	18	3	6	9	11	11	4	18	5
Mutagenicity	8	23	41	38	1	2	21	25	15	6	29	24
Fish toxicity	3	9	13	9	1	2	10	12	7	3	16	13
Daphnia toxicity	1	3	6	6	1	2	4	5	3	1	4	3
Biological accumulation or biological degradation	0	—	9	8	0	–	5	6	6	2	11	9

SOURCE: Office of Technology Assessment.

in volumes equal to or less than those proposed for exemption by EPA.

The skewing of production volumes toward higher values is most noticeable for polymers being produced for nonconsumer uses (table 20). Seventy-six percent of all nonconsumer-use polymers are slated for production in volumes greater than 10,000 kg annually.

The frequency of submission of toxicity data for nonconsumer-use polymers tends to decrease with increasing projected production volumes. An easy-to-hand suggestion to explain that tendency is that large production volume non-consumer-use substances are often "me too" chemicals. Manufacturers might be well acquainted with the properties of closely related substances and satisfied with estimates of toxicity based on them. Apparently EPA is also satisfied with those estimates.

MAGNITUDE OF SCALE-UP IN PRODUCTION OF LOW-VOLUME CHEMICALS

Because of concerns about confidential business information, OTA did not collect precise estimates of first- and third-year production volumes. Instead, first year production was collected as:

1. 1,000 kg or less,
2. 1,001 kg to 10,000 kg, and
3. greater than 10,000 kg.

Third year production volume was recorded as a multiple of the first year volume:

1. Less than a fivefold increase,
2. fivefold to tenfold increase,
3. twentyfold to fiftyfold increase,
4. fiftyfold to hundredfold increase,
5. hundredfold to two hundredfold increase, and
6. greater than two hundredfold increase.

Table 21 shows the expected scale-up of production of chemicals from each of the initial year production volumes. Also shown are estimates of the kilograms of each chemical to be expected in the third year. These estimates are necessarily imprecise because exact production volumes were not recorded. Instead, as is shown on the table, an initial year production volume of 500 kg was assumed for the less than 1,000 kg class, 5,000 for the 1,001 to 10,000 kg class, and 10,001 (rounded down to 10,000) for the greater than 10,000 kg

Table 21.—Estimated First Year Production Volumes, and Increases Expected in the Third Year

Initial year production volume	Increase in third year		Estimated[a] first year product ion (kg)	Estimated third year product ion (kg)
<1,000 kg	< 5-fold[b]	101	500	500-2,500
	5- to lo-fold	23	500	2,500-5,000
	10- to 20-fold	11	500	5,000-10,000
	20- to 50-fold	5	500	10,000-25,000
	50- to 100-fold	0	500	—
	100- to 200-fold	4	500	50,000-100,000
	> 200-fold	11	500	>100,000
		135		
1,001 kg to 10,000 kg	<5-fold	81	5,000	5,000-25,000
	5- to 10-fold	41	5,000	25,000-50,000
	10- to 20-fold	11	5,000	50,000-100,000
	20- to 50-fold	9	5,000	100,000-250,000
	50- to 100-fold	6	5,000	250,000-500,000
	100- to 200-fold	2	5,000	500,000-1,000,000
	> 200-fold	0	5,000	—
		150		
>10,000 kg	c 5-fold	193	10,000	10,000-50,000
	5- to 10-fold	50	10,000	50,000-100,000
	10- to 20-fold	11	10,000	100,000-200,000
	20- to 50-fold	3	10,000	200,000-500,000
	50- to 100-fold	1	10,000	500,000-1,000,000
	100- to 200-fold	7	10,000	1,000,000-2,000,000
	> 200-fold	0	10,000	—
		265		

[a] *See* text.
[b] For brevity the increases are written as 5- to 10-fold, 10- to 20-fold, etc. In practice, 5-to 10-fold means equal to or greater than 5 and less than 10, 10- to 20-fold means equal to or greater than 10 and less than 20, etc.

SOURCE: Office of Technology Assessment.

class. The assumption of 500 for the first class and **5,000** for the second class may be either high or low; the assumption of 10,000 for the third must be low.

In all three classes, production of more than half of all the chemicals increases less than fivefold. At the other end of the production increase scale, 15 of the 155 less than 1,000 kg initial year production volume chemicals are expected to increase by at least 50 times in the third year. The comparable fraction for the 1,001 to 10,000 kg class is 8/150; for the more than 10,000 kg, 8/265.

EPA expects to require PMN review for low-volume chemicals when their production increases to at least **10,000** kg per year. It is impossible to predict, from OTA's collected data, what number of PMNs report chemicals that will increase to 10,000 kg production volumes in the third year. However, if all chemicals in the less than 1,000 kg per year class that increase by 20-fold or more have an initial production of at least 500 kg, then 20 of the 155 chemicals of that class will require PMN review in the third production year. For the 1,001 to 10,000 kg class, if all the chemicals that increase in production at least fivefold have first year production volumes of at least 5,000 kg, 69 of the I50 will require PMN review in the third year. These estimates suggest that many chemicals exempted from PMN review because of low production volume when they are first introduced will be subject to review in their third year of production.

ARE PMNs SUBMITTED FOR IMPORTED CHEMICALS MORE COMPLETE THAN THOSE SUBMITTED FOR OTHER CHEMICALS?

The European Economic Community (EEC) has adopted a base set of tests that are required before a new substance can be marketed in member countries. It is not an overstatement to contrast the EEC and the Toxic Substances Control Act (TSCA) requirements by saying that EEC demands that several kinds of test data be submitted unless an exemption is granted; TSCA does not authorize EPA to require generation of test data unless EPA lacks information to make a determination about some unreasonable risk that the substance may present.

No impact of the EEC requirements would be expected on the PMNs examined by OTA because they were not in effect in 1979 and 1980. Nevertheless, the PMNs that described imports were examined separately. A comparison of import PMNs to all other PMNs is shown in table 22. The frequency with which chemical identification data were submitted was essentially 100 percent for both domestic and imported PMNs, but imports less frequently reported byproducts, numbers of workers, and disposal (data not shown). Those smaller numbers may largely be explained because byproducts, workers, and disposal methods in foreign countries are not a concern for the United States EPA.

As is shown on table 22, neither physical-chemical nor toxicity data were consistently reported more frequently on the import PMNs. Seven of the eleven physical-chemical items were more frequently present on domestic PMNs; **6** of the 11 toxicity items.

Table 22.—Physical-Chemical and Toxicity Information Submitted for Import PMNs and All Other PMNs

	Imports		All other PMNs	
	No.	Percent	No.	Percent
Physical-chemical Information:				
PMNs .,	63	100	677	100
Infrared spectra	4	6	82	12
Purity.	45	71	498	74
Analytical methods	46	73	368	54
Melting point	24	38	155	23
Boiling point	12	19	207	31
Density	10	16	130	19
Vapor pressure	9	14	171	25
Volubility (water)	30	48	278	41
Partition coefficient	2	3	25	4
Transportation	53	84	429	63
Emergency information	21	33	234	35
Toxicology information:				
Acute oral toxicity	35	55	285	42
Acute dermal toxicity	12	19	210	31
Acute inhalation toxicity	2	3	65	10
Skin irritation	23	36	227	*34*
Skin sensitization	3	5	63	*9*
Eye irritation	22	35	254	*38*
Repeated dose toxicity	4	6	82	*12*
Mutagenicity	15	24	112	*17*
Fish toxicity	13	21	51	*8*
Daphnia toxicity	1	2	28	4
Biological accumulation or biological degradation	9	14	27	4

SOURCE: Office of Technology Assessment.

Actions Taken by the Environmental Protection Agency as a Result of Reviewing Premanufacture Notices

8. Actions Taken by the Environmental Protection Agency as a Result of Reviewing Premanufacture Notices

The heart of any questioning about the Premanufacture Notice (PMN) program is whether it has protected human health and the environment from unreasonable risks. A partial answer to that question will become available in the years to come as information is accumulated about the health and environmental effects of substances that passed through PMN review and then entered commerce. In the meantime, a less satisfactory answer to questions about the accomplishments of the PMN program can be obtained by examining actions that the Environmental Protection Agency (EPA) has taken to reduce exposures to chemicals that may present unreasonable risks.

From among the PMNs examined by OTA, nine described chemicals that did not begin manufacture because of formal EPA actions. Six of those described phthalates, which at the time of review were especially suspect because of a then-recently completed National Cancer Institute test that showed some phthalates to be carcinogenic **(9).** Two of the remaining three were benzidine dyes, which have long been associated with human carcinogenicity. The fact that the benzidine dyes were submitted shows that some chemicals strongly associated with human toxicity are considered for manufacture.

EPA's insisting on more tests for those nine chemicals prevented their being manufactured. In those cases, when EPA issued a 5(e) order, the submitter decided not to submit the requested information and withdrew the PMN. The reasoning behind the submitters' decisions is not known and may differ depending on the chemical and the submitter. However, when EPA determined that the new chemical might present an unreasonable risk, the submitting company may have agreed that the chemical was more likely than not to harbor some hazard, and that further testing might confirm the hazard.

If a submitting company decided to execute the EPA-requested tests, the tests might confirm that the chemical is hazardous. In that case, the submitter cannot manufacture the chemical and is out the money spent on developing test data. If the test data are equivocal and neither confirm the hazard nor dispel it, the submitter is also out the cost of the test. He also faces another decision about whether or not to produce more data at more cost in the expectation that more data will resolve EPA's concern about the chemical. The third possible outcome is that the EPA-requested test data show that the chemical is not hazardous and that production of the chemical can commence. In that case, for the cost of the test, the submitter gains access to the market for those chemicals.

Industry reviewers of the first draft of this background paper expressed their conviction that the cost of the required tests alone, with no consideration of the possible outcomes, was sufficient to convince the submitting companies to withdraw the PMNs. Instead of spending the money on the tests, it might be better spent on developing other chemicals.

Such activities are to be expected as a result of TSCA and implementation of its provisions to regulate new chemicals. The law provides that chemicals that are suspected of being toxic are to be identified before manufacture and prevented from being manufactured unless sufficient data are produced to show that the toxicity does not present an unreasonable risk.

Three additional 5(e) orders have been written (two in **1982;** one in **1983).** The two in **1982** were "consent 5(e)'s, " which represented an agreement

between the submitter and EPA that manufacture of the substances would be restricted and that the company would not challenge the order in court.

In addition to the 5(e) orders, EPA had achieved 54 "voluntary regulatory" actions through the first three quarters of 1982. In those cases, EPA requested that a submitter develop additional information or impose voluntary controls. Table **23** is from an EPA memo dated July **30, 1982 (6).** It shows results that EPA has obtained through its "informal regulatory actions" from the beginning of the program through June **1982.**

The memo **(6)** briefly describes each of the informal actions. Examples of each type of action are discussed here:

- *Voluntary Testing* **(12** cases). -In one case, EPA was concerned about the mutagenicity of the chemical. The submitter performed a bacterial mutagenicity test (see table 11 and accompanying text for discussion, also (9)) and the results were positive. The company complied with a request to affix warning labels to containers of the chemical to alert workers to a possible health hazard.
- *Voluntary Controls* **(26** cases) .-Most of the actions involved developing an appropriate warning label. For example, a PMN described a chemical for use by home hobbyists. EPA notified the submitter of its concerns about possible dermal absorption. The submitter labeled the chemical bottles with directions that rubber gloves be worn. In addition to such voluntary labeling actions, some companies have agreed to reduce exposures during manufacture and, in one case, not to manufacture a particular group of chemicals.
- *Major Pending Negotiations Under Suspended Review Notice (13* cases).—In these cases, EPA has negotiated with the submitter to produce additional toxicity information. The review period was suspended because the execution and analysis of tests would extend beyond the 90-day review period. Upon completion of the tests and their submission to EPA, the review "clock" can be restarted from where it was stopped.
- *Withdrawal of PMN in Face of Likely 5(e) Order (2* **cases).—** In one case, EPA decided to write a 5(e) order because of large production volume and substantial potential exposure and release. The company, when notified of EPA's intention to write a 5(e) order to require testing, withdrew the PMN.
- *Withdrawl of PMN in Face of Likely 5(f) Order (1* **case).** —A 5(f) order can be written when EPA decides that a substance presents or will present an unreasonable risk to health or the environment. When the submitting company learned that EPA was preparing to regulate the substance under section 5(f), it withdrew the PMN "stating that it did not wish to be the target of EPA's first TSCA section 5(f) order" **(6).**

These voluntary regulatory efforts have generated additional information, controlled exposures, and caused the withdrawal of PMNs that described chemicals that caused EPA concern. During the time the 54 voluntary actions occurred, EPA received a total of 1,499 PMNs. In other words, voluntary regulatory actions accompanied about 3.6 percent of those PMN reviews.

Table 23.-EPA Summary of Informal Regulatory Actions in Fiscal Years 1979, 1980, 1981, and First Three Quarters of Fiscal Year 1982

	Fiscal year 1979	Fiscal year 1980	Fiscal year 1981	Fiscal year 1982	Total
Informal action—voluntary testing	0	1	8	3	12
Informal action—voluntary controls	0	1	12	13	26
Major pending negotiations under suspended review period	0	0	0	13	13
PMNs withdrawn in face of likely 5(e) order	0	1	1	0	2
PMNs withdrawn in face of likely 5(f) order	0	0	0	1	1
Total	0	3	21	30	54

SOURCE: Environmental Protection Agency (1982).

In summary, EPA has taken action on 66 PMNs (12 formal 5(e) orders and 54 voluntary compliance). Whether that is an appropriate number depends on the opinion of the observer. If the observer considers most chemicals to be without hazard, taking action on about 4.4 percent of all PMNs may seem too high or just about right. On the other hand, that percentage of actions may seem too low to an observer who considers that a larger fraction of chemicals are hazardous. Thus, the implication of the percentage is a matter of interpretation.

This paper focuses on the frequency with which PMNs report various kinds of data to EPA. It points to groups of PMNs for which EPA received more or less information, but it has not delved into how EPA used the submitted information and other information in making decisions not to take any action, in which case manufacture went ahead unimpeded, or to take action to restrict manufacture or limit exposure. The last chapter of this paper (ch. 9) outlines a possible method to investigate EPA's decisionmaking process and its use of the information submitted on PMNs.

9 m

Discussion

9 Discussion

FREQUENCY OF REPORTING OF INFORMATION ON PREMANUFACTURE NOTICES

OTA inspected 740 premanufacture notice (PMN) files to determine what items of information have been submitted to the Environmental Protection Agency (EPA). The presence or absence of three kinds of information was recorded:

1. information specified by the Toxic Substances Control Act (TSCA) (seven items),
2. information that describes the physical-chemical properties of the chemical (11 items),
3. information about the toxicity of the chemical (11 items),

The results presented in this background paper place limits on possible answers to questions about how much information EPA has received on PMNs. The reporting of TSCA-specified items is high. Six of the seven specified items—chemical identity, chemical class, production volumes, uses for the chemical, numbers of workers likely to be exposed in their places of employment, and disposal methods—were reported on more than 90 percent of all PMNs. The seventh specified item, information about byproducts generated in the manufacture of the chemical, was reported on about two-thirds of all PMNs (table 3). Ninety-six percent of all PMNs reported at least one item of non-TSCA specified physical-chemical information (table 7). Fifty-three percent reported at least one toxicity test result (table 12). The other side of the last observation is that 47 percent of all PMNs, almost half, reported no toxicity data.

The reporting of both physical-chemical and toxicity data was more frequent on PMNs that described chemicals that are known to be present in commerce as compared to chemicals that, so far as is known, have not actually entered commerce (tables 7 and 12). Those findings are important because exposure is certainly greater to manufactured chemicals. Nevertheless, 41 percent of PMNs that described manufactured chemicals reported no toxicity data.

About 10 percent (70 of 740) of the PMNs examined here were submitted in June 1982. The frequency of reporting of toxicity data on those PMNs was lower than the frequency on all PMNs, both those that described manufactured and not-yet-manufactured chemicals, received during the 1979 through June 1981 period. In contrast, 4 of the 11 physical-chemical items examined by OTA were reported most frequently on June 1982 PMNs.

The lower frequency of toxicity test reporting in June 1982 might be considered an aberration and not reflective of a downward trend. Alternatively, it might be taken as a harbinger of decreased toxicity testing. A decision can be made between these two points of view by examining PMNs received during other months. EPA's establishing a program to monitor and report the information content of PMNs on an ongoing basis might be the best way of tracking the frequency of reporting of specific information on PMNs.

DATA SUBMITTED ON PMNs THAT DESCRIBED CHEMICALS INTENDED FOR CONSUMER USE

Consumer-use chemicals are of special interest because of their use by many people, which results in widespread exposure. Of the PMNs examined by OTA, 105 (14 percent) were designated by the submitting companies as being intended for consumer use.

OTA's examination of consumer-use PMNs concentrated on the frequency of reporting of toxicity data. Fifty-seven of the consumer-use PMNs described nonpolymers, and 47 described polymers (table 19). Reporting of toxicity data on both consumer use polymers and nonpolymers was more frequent than for the corresponding nonconsumer-use chemicals (compare tables 19 and **20).**

Acute oral toxicity was reported on 70 percent of the PMNs that described consumer use, nonpolymer chemicals to be made in excess of 10,000 kg annually (table 19). That frequency is the highest reporting frequency of any type of toxicity information for any subgroup of PMNs examined here. It suggests that these substances were singled out for special concern, perhaps because of the high-exposure potential. Despite the high frequency of reporting of acute oral toxicity, mutagenicity data were reported on only 17 percent of the high-volume, nonpolymer, consumer-use chemicals. That frequency is the same as that found for all PMNs taken together (table 12), and it highlights the low frequency of reporting data about chronic health effects.

DATA SUBMITTED ON PMNs THAT DESCRIBED CHEMICALS PROPOSED FOR EXEMPTION FROM PMN REVIEW

EPA has proposed exempting some categories of chemicals from PMN reporting: 1) some polymers, 2) site-limited intermediates, and 3) chemicals to be manufactured in low volumes. Not all polymers, site-limited intermediates, or low-volume substances would qualify for exemption (see ch. 2), but many would. OTA examined separately PMNs that had been identified by submitters as polymers, site-limited chemicals, and low-volume chemicals.

The polymer exemption is premised on the idea that those substances, in general, are less likely than other chemicals to be toxic. Consistent with that idea, PMN submitters reported and evidently developed fewer toxicity data for polymers than for other classes of chemicals (tables 14, 18, 19, and 20).

The proposed exemptions for site-limited intermediates and low production volume substances are based on the idea that limited exposures associated with those substances reduce risk. Therefore, EPA proposes that it needs less information to make a decision about those substances.

OTA's examination of PMNs shows that toxicity information was more commonly submitted for site-limited chemicals than for all other chemicals (table **16** and fig. 8). Although the number of people who might be exposed to those chemicals is limited, levels of exposure conceivably are quite high. Since EPA does not require the generation of test data, the submitting companies apparently develop such information for their own use. Whether or not toxicity data would be developed for these substances with the same frequency if the exemption becomes final is, of course, unknown. Of course, the data would no longer be submitted to EPA.

PMNs describing chemicals to be made in volumes of less than 1,000 kg per year reported toxicity data more frequently than did PMNs describing other chemicals (table 17 and fig. 9). More detailed analysis showed that polymer PMNs tended to project greater production volumes (tables 18-20), and the reduced reporting of toxicity data for polymers at least partially accounted for the more frequent reporting of toxicity data on low-volume PMNs. Data about expected increases in production volume suggest that about a one-third of the low-volume exemption substances will require a PMN review by their third year of production due to their exceeding the 10,000 kg annual production mark (table 21).

The proposed polymer exemption, to some extent, acknowledges the present situation. Apparently because those substances are thought to be less hazardous, fewer toxicity data are submitted about them.

The site-limited intermediate and low-volume exemptions are more complex. Toxicity data are more frequently submitted on PMNs that describe those chemicals. Whether those data would be developed for the company's own use with the same frequency under an exemption policy is unknown, although it appears likely. Additionally, more knowledge of the exact content of the PMNs is necessary to know if the submitter-identified site-limited and low-volume chemicals would qualify for the proposed exemptions.

In the absence of a substantial amount of additional information, OTA can come to no definite conclusions about either the proposed exemptions or the overall adequacy of EPA's PMN program. The results reported here do, however, provide information about the number of data received by EPA.

If the reader generally believes that most chemicals chosen by companies for manufacture are not hazardous under company-specified conditions of use and with appropriate safeguards, then, certainly, the proposed exemptions will be seen as desirable and efficient. If the reader does not share that general viewpoint, then a critical question can be asked about whether the companies will generate toxicity information under the proposed exemptions, and a decrease in data would be seen as harmful.

USEFULNESS OF SUBMITTED INFORMATION FOR EPA's RISK ASSESSMENT PROCESS

EPA's list of items to be considered in evaluating a chemical's risk (see app. A) shows that every item of physical-chemical and toxicity information considered in this report can be of use in reviewing PMNs. However, not every item is necessarily required for the review of every PMN. The critical question is whether the information received for EPA review was sufficient, and the analysis necessary to answer that question goes beyond this OTA examination.

A related question stems from the absence of toxicity data and EPA's use of Structural Activity Relationship (SAR) analysis (see ch. 2). Regulatory actions to remove pesticides from the market have made it clear that tests on the exact product, not closely related chemicals, are necessary to ban or restrict production. Therefore, there seems to be little dependence on SAR in those decisions. Pesticides are, by nature, active in some biological systems, and greater care is necessary for their use than for chemicals in general. So, on the one side, SAR is not sufficient to regulate closely related chemicals of classes known to be biologically active.

SAR is used to estimate the physical-chemical, and toxic properties of substances when PMNs contain no data. Few chemicals are toxic under normal conditions of use and the presumption can be made that most new chemicals present no or minimal hazard. Therefore, the use of SAR, which depends on using information about related chemicals to estimate the hazard of the new chemical, may be more appropriate for new chemicals.

At the same time, it must be recognized that SAR is in its infancy. Its current level of use in the PMN program may be correct, too high, or too low. In any case, careful attention to its use, its successes and failures, is necessary to define situations where its use is or is not appropriate.

Industry reviewers of the first draft of this background paper stated that physical-chemical and toxicity data are obtained to enable the submitting company to process and manage the new chemical. Those data, collected by the company and submitted to EPA, are seen by industry as sufficient for EPA review of PMNs. It is not entirely clear that all such data are reported. For instance, only **38** percent of Class 1 substances (chemicals that can be represented by a chemical formula or structure) reported melting points; **24** percent reported boiling points (tables **6** and 9). One or the other or both of these measurements might be expected on every Class 1 chemical.

Information collected by EPA suggest that factors other than a company's need for information

may influence the reporting of data on PMNs. In particular, an EPA analysis (2) showed a clear correlation between submission of more data and larger company size, regardless of whether the company was or was not primarily a chemical manufacturer. In 1981, EPA estimated that running tests, collecting, and submitting the physical-chemical and toxicity data of the types that OTA looked for would cost between $53,000 and $67,850 (table 24) per chemical. (Earlier, EPA had estimated that the costs of *submitting* a PMN, which included collecting and organizing existing data but not the costs of testing, would be in the range of $1,555 to $15,325 (44 F.R. 59767, Oct. 16, 1979).)

Two tests of particular value are partition coefficient tests that measure the relative affinities of a chemical for aqueous and organic environments and mutagenicity tests that measure interactions with DNA. These are not often reported on PMNs (5 and 17 percent respectively, tables 9 and 12), and they are not a major part of the costs associated with the full set of tests shown in table 24. All of the physical chemical tests, including determination of the partition coefficient, are estimated to cost $3,800, and mutagenicity tests are estimated to cost $1,350 for the simple bacterial tests (table 24).

In general, industry reviewers of the first draft of this background paper were approving of the PMN program. They see it as doing an adequate job of protecting health and the environment, and they looked with favor on the proposed exemptions.

Environmental organization reviewers, however, equally emphatically stated that absence of data, especially toxicity data, causes EPA to "swallow uncertainty" too often and to fail to discharge properly its duties under TSCA. They urged that EPA insist on obtaining more toxicity data, and some argued that EPA should require submission of a base set of data, similar to that required by the European Economic Community (46 F.R. 8986).

Table 24.—Estimated Costs of Tests That Might Be Reported on PMNs

Type of data	Estimated cost
Physical/chsmical data:	
Data about 11 characteristics	$3,600
Acute toxicity data:	
Acute oral toxicity	2,000
Acute dermal toxicity	2,800
Acute inhalation toxicity	3,300
Skin irritation	700
Skin sensitization	3,200-6,700
Eye irritation (for chemicals showing no skin irritation)	450
Repeated dose toxicity data:	
14- to 28-day-repeated dose test(s) using probable route(s) of human exposure	10,200-12,800
Mutagenicity data:	
Gene (point) mutation data	1,350
Chromosomal aberration data	18,000
Ecotoxicity data:	
Data about killing of three lower organisms	4,100
Degradation/accurnu/at/on data	*3,100-11,850*

SOURCE: Office of Technology Assessment, 1981.

POSSIBLE FURTHER EVALUATION OF THE PMN REVIEW PROCESS

Some industry reviewers of the first draft of this background paper praised EPA for recruiting a competent staff for the PMN review program. They expressed satisfaction that many of the Office of Toxic Substances' staff exercise what the industry reviewers see as "proper professional judgment" in their duties.

EPA employees who review PMNs speak of "swallowing uncertainty" when they make decisions with insufficient data. No amount of inspecting records of the amount of data submitted on PMNs, as was done here, can reveal the frequency with which the data submitted on a PMN were sufficient for adequate review.

There must be cases in which EPA exercised "professional judgment" or "swallowed uncertainty" when data were limited among the PMNs examined by OTA. A surer base for conclusions about the adequacy of PMN data submission and use could be provided by an examination of: 1) the EPA's use of the submitted data, 2) the Agency's decisions to ask or not to ask for more

information, and 3) the appropriateness of the Agency's deciding to use or not to use SAR analysis when data were not available. Such an examination would require evaluation of the suitability of the PMN data and careful inspection of written records and interviews of EPA officials to describe the decisionmaking process.

Clearly, not all PMNs, not even many PMNs, could be examined in that depth. A sample of some of the PMNs that resulted in a regulatory action or a voluntary restriction (see ch. **8)** could be examined to learn about the processes and decisions that resulted in an EPA action. Equally, perhaps more, important, a selection of PMNs that resulted in no EPA action would also have to be examined. PMNs that described chemicals of high potential concern-some to be made in very large amounts and for consumer use (see table **19),** or polymers to be excluded from the proposed exemption (see table 2), or chemical classes known to be highly reactive or biologically active—could be selected. The selection process would be critical because a charge likely to be leveled an any analysis is that the PMNs chosen for study were not representative.

The study should include a careful look at the quality of the submitted data, the steps that EPA took to find additional data, and an effort to see if other data were readily available. If SAR analysis was used by EPA, the study should examine the bases for the decision to use that technique, the appropriateness of EPA's efforts to gather information on related chemicals, and the reasonableness of the decisions made by EPA.

An analysis of this sort, if not limited to a few PMNs, could involve amounts of staff and resources rivaling those used for PMN review by EPA. It would require various kinds of experts and access to diverse sources of data. The cost might be so high as to be prohibitive. At the same time, such an analysis might be necessary to decide if EPA's decisions about unreasonable risks were reasonable.

Appendixes

Appendix A.—Summary of Topics Considered at Evaluation Meeting During Initial Screen of Premanufacture Notices at the Environmental Protection Agency

I. General Information for PMN Substances
- **A. Manufacturing Process and Chemistry**
- **B. Physical-Chemical Properties**
  - **1. Composition**
  - **2, Physical form (solid, liquid, gel, etc.)**
  - **3. pKa ionization constant**
  - **4. Partition coefficient (affinity for aqueous and organic solvents)**
- **C. Use Function**
  - **1. Known and potential uses**
  - **2. Production capacity and potential growth**
- **D. Regulatory Concerns**

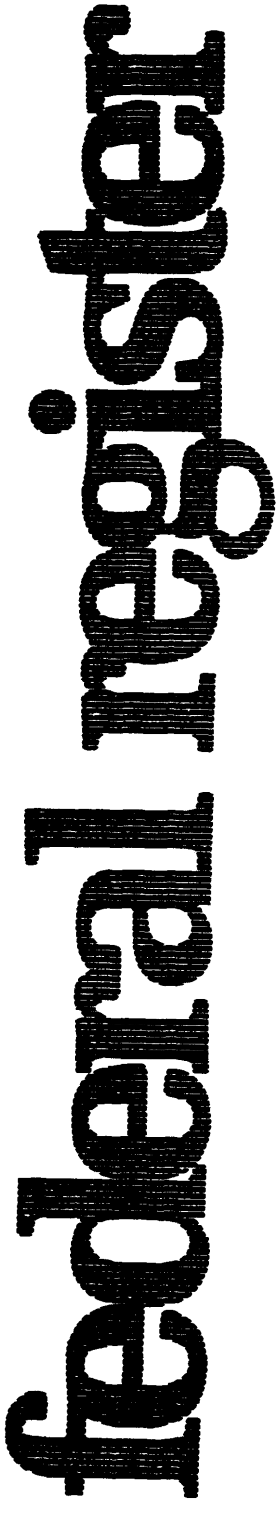
II. Assessments
- **A. Structural Activity Team Report**
- **B. Health Hazards**
  - 1. Metabolism, uptake, excretion
  - 2. Acute toxicity
    - a. LD_{50} (amount of chemical necessary to kill 50 percent of test animals)
    - b. Other acute effects
  - 3. Carcinogenicity, mutagenicity, teratogenicity
  - 4. Other chronic effects
- C. Ecological Hazards
  - 1. Effects on microbes
  - 2. Effects on invertebrates
  - 3. Effects on plants
  - 4. Effects on fish
  - 5. Effects on mammals and birds
  - 6. Effects on ecosystem process
- D. Worker/Consumer Exposure
  - 1. Worker exposure from manufacture
  - 2. Worker exposure from processing
  - 3. Consumer exposure
- **E. Environmental Release**
  - **1. Release from manufacture**
  - **2. Release from processing**
  - **3. Release from use**
  - **4. Release from disposal**
- **F. Environmental Fate**
  - **1. Persistence**
    - **a. Degradation**
    - **b. breakdown products**
- **G. Non-Risk Factors**
  - *1.* Company size and characteristics
  - **2.** Substitutes (for the new chemical and old chemicals that the new chemical may substitute for)
  - **3.** Potential new uses
  - **4.** Financial effect of the PMN chemical on company
  - **5.** Benefits to society

HI. Summary of Outstanding Problems of Scientific/ Technical Concerns
- **A, Most Serious Problem**
  - 1. **Health hazard**
  - **2. Ecological hazard**
  - **3. Worker/consumer exposure**
  - **4. Environmental release**
  - **5. Environmental fate**
  - **6. Non-risk factor**

IV.
- A. Related Substances
- B. Solvents (used **in manufacture and processing)**
- **C. Catalysts (used in manufacture and processing)**
- **D. Byproducts (from manufacture and processing)**

V. Priority Problem in Profile

Appendix B.—Copies of Face Sheets: EPA and CMA PMN Forms



Tuesday
October 16, 1979

Part III

Environmental Protection Agency

Reproposal of Toxic Substances Control Act (RCA) Premanufacture Notice (PMN) Forms and Provisions of Rules

APPENDIX A

PREMANUFACTURE NOTICE FORM

PROPOSED BY

MANUFACTURING CHEMISTS ASSOCIATION

NOTE: **Copies of the compiete form can be obtained from the Chemicai Manufacturers Association, 2501 M St., NW, Washington, D.C., 20037.**

Appendix C.—Acknowledgments

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Appendix D.—Acronyms and Glossary

Acronyms and Glossary

5(e) order.—A formal regulatory order from EPA stating that a chemical may pose an "unreasonable risk," restricting its manufacture, use, or disposal, and stipulating tests that have to be performed to satisfy the Agency that the chemical does not pose such risks.

carcinogen.-A substance or agent that causes cancer.

CBI.—Confidential Business Information.

Class I substance or chemical.-A chemical that can be represented by a chemical formula and structure.

Class II substance **or chemical.—A complex chemical combination that cannot be represented by a chemical formula or structure.**

Class 111 substance or chemical.—A polymer.

CMA.—Chemical Manufacturers Association.

daphnia.—Minute freshwater crustaceans.

ecotoxicity.-The property of causing harm to biota—plants, animals, or microbes—in the environment.

EEC.—European Economic Community.

EPA.—Environmental Protection Agency.

Inventory of Chemical Substances. -An EPA-compiled list of all chemicals, subject to the provisions of TSCA, that are present **in U.S. commerce.**

kg.–kilogram (about 2.2 **pounds).**

manufacture.—In this study, the manufacture or **importation of a "new" chemical. This legally can take place only after PMN review.**

MPD.—Minimum Pre-Marketing Data set, a data set required by the EEC before a chemical can be manufactured within those countries.

mutagen.—A substance or agent that interacts with DNA, the genetic material, and produces heritable changes.

"new" substance or chemical .-A substance or chemical not listed on the Inventory Chemical Substances.

NOC.—Notice of Commencement: a notice sent to EPA to notify the Agency that manufacture of a "new" chemical has begun.

OECD.—Organization for Economic Cooperation and Development.

OTA.—Office of Technology Assessment.

OTS.—Office of Toxic Substances, EPA.

PMN.—Premanufacture Notice.

Manufactured PMN.—In this study, a PMN received by EPA before the end of June 1981 that completed review by the end of September 1981 and that described a chemical which began manufacture before the end of August 1981.

Nonmanufactured PMN.–In this study, a PMN received by EPA before the end of June 1981 that completed review by the end of September 1981 and that described a chemical which had not begun manufacture by the end of August 1981.

Regulated PMN.—In this study, a PMN that resulted in EPA writing and issuing a S(e) order requiring the PMN submitter to produce data about the chemical.

June 1982 PMN.–In this study, any PMN received by EPA in June 1982.

polymer.—A chemical that is composed of repeating, simpler chemical subunits (and see ch. 4).

review period.—The 90 **days after EPA receives a PMN. If EPA does not find that the PMN describes a chemical that may present an unreasonable risk, manufacture may begin after 90 days.**

SAR.-Structural Activity Relationship analysis, techniques for estimating chemical and biological activities of a chemical substance based on knowledge of related chemicals.

teratogen.—A substance or agent that causes birth defects.

TSCA.—Toxic Substances Control Act.

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