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Discussion

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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.