United States General Accounting Office 144919

GAO Testimony

For Release
on Delivery
Expected at
9:30 a.m.
Wednesday
Oct. 2, 1991

Reproductive and Developmental Hazards: Regulatory Actions Provide Uncertain Protection

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Before the
Committee on Governmental Affairs
U.S. Senate

Mr. Chairman and Members of the Committee:

It is a pleasure to be here to share with you the results of GAO's work regarding federal regulatory control of toxicants that cause adverse reproductive and developmental outcomes. Our study comes at a time when there appears to be rising concern about the impact on individuals, families, and society of these toxicants.

Mr. Chairman, this Committee had the foresight to request that GAO look at these issues when many people were still unaware of their importance. Yet the effects of the exposures we deal with in this study contribute to some of the most difficult national challenges we face today. These include the large number of infants born with birth defects along with the costs of their life-long care, the high U.S. infant mortality compared to other developed countries, and a growing number of children with basic learning disabilities. The causes of 60 percent of these and other reproductive and developmental diseases are currently unknown and the exact percentage caused by environmental exposures may not be known for decades. However, it is obvious that with grave events such as these, prevention is preferable to treatment, and chemical exposures are probably the most preventable of the known causes.

The network of federal programs authorized to control exposure to toxicants has the major responsibility to prevent environmentally caused disease. You asked us, therefore, to study the extent and

sufficiency of federal regulation of reproductive and developmental hazards by answering four questions:

-- What are the environmental chemicals of high concern for causing reproductive or developmental disease?

-- To what extent are these chemicals regulated by the federal government?

-- To what degree are the regulations based on reproductive or developmental toxicity?

-- Does federal regulation for these chemicals provide sufficient protection from reproductive and developmental disease?

Let me begin by briefly highlighting the three key results of our study and then go on to give the answers to these four questions in some detail.

First, federal regulatory agencies have not consistently applied the scientific knowledge that exists to the control of the reproductive and developmental hazards of environmental chemicals. Instead, the major federal regulatory efforts appear to have focused on cancer and acute toxicity.

Second, across the 10 programs we reviewed, the regulatory achievement on 30 widely acknowledged reproductive and developmental hazards falls short of the professed standards of these very programs and those of experts. These shortcomings include the failure to regularly examine and consider reproductive and developmental toxicity data during regulatory decision-making.

Finally, looking across a number of indicators, the sufficiency of protection afforded by the current regulation of reproductive and developmental hazards is in doubt, both for the 30 we studied and quite possibly for other chemicals as well.

Background

Generally, reproductive diseases are those that impair the ability of men or women to conceive, while adverse developmental outcomes affect the growing child from conception on. In spite of severe limitations on data, the estimates that do exist suggest significant problems. Birth defects are the single largest attributable cause of infant mortality in the United States--accounting directly for 20 percent. In 1988, over 250,000 U.S. children were born with diagnosed birth defects. Many other outcomes, such as learning disabilities, become evident only at later ages. Still other adverse effects such as infertility and miscarriage are far more common than generally realized; an estimated 8 percent of U.S. couples are infertile and 600,000 miscarriages are diagnosed and

reported each year. These figures underestimate the dimension of the problems, since both infertility and miscarriages are underreported. Currently, quantitative estimates of conceptions that end in miscarriage range from 30 to 80 percent.

The Science of Reproductive and Developmental Toxicity

The field of reproductive and developmental toxicity is a very young science. Although the deleterious--and now well-known--effects of lead and alcohol have been suspected for centuries, only with the terrible discovery of the drug thalidomide's effects in the 1960s did the field begin to develop as a cohesive scientific endeavor. This means that data collection and understanding of the basic phenomena still lag several decades behind our specific knowledge of cancer, for example.

Research linking environmental cause and human disease is difficult, involving as it does, the complications of exposures undergone by no less than three relevant parties: the mother, the father,and the child. Not surprisingly, several of the best researched toxic agents are drugs. Two examples are thalidomide and diethylstilbestrol (DES), which caused limb deformities and cancer, respectively, in offspring. In cases of prescribed drugs, doses are often known precisely and the outcomes are dramatic and well defined. A nondrug example with a distinct outcome is DBCP, a pesticide that produced absolute male infertility through occupational exposure.

But most exposures are hard to measure and most outcomes are not easily linked directly to an environmental agent. Thus, the well-established reproductive and developmental hazards may be only the tip of the iceberg.

Because of these difficulties, the most common source of information about reproductive and developmental toxicities is from live animal tests. Several hundred toxicants have been found to produce adverse reproductive effects in one or more experimental animals, but since no single animal species is a perfect predictor for effects in man, it has been difficult to develop a protocol to identify which toxicants should be considered potential human hazards. In general, however, animal studies have reasonably good predictive value for man.

Only 3 percent of human reproductive and developmental disease can now be directly attributed to environmental chemicals. However, the National Research Council believes that some of the disease with no attributable cause will be found to be environmentally induced. Thirty-seven percent of the experts we surveyed predicted between 10 and 25 percent will be found to have an environmental origin, while another 37 percent predicted a higher proportion will be environmentally caused. Since chemical exposure is clearly preventable, a priori, we focused on that particular cause of reproductive and developmental disease in our evaluation.

Study Design and Methods

As already noted, the purpose of our study was to examine the effectiveness of federal regulatory control of environmental reproductive and developmental hazards. To this end, we looked at the regulatory performance of 10 federal offices in four regulatory agencies--Consumer Product Safety Commission, Environmental Protection Agency, Food and Drug Administration, and Occupational Safety and Health Administration.

The first step in the study was the identification of a list of those environmental chemicals that were the best known and most widely acknowledged as causes of reproductive or developmental disease. We reasoned that federal action on these chemicals would show regulatory performance at its best and serve as an indicator, overall, of the caliber of current regulatory protection against reproductive and developmental toxicants.

Recognizing the limits of knowledge in this relatively new field, we chose a conservative approach depending on both published scientific reviews and experts in the field.[1] In essence, the

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[1]In acknowledgment of uncertainty in the field, we strove for a convergence of scientific opinion, rigorously using systematic rules to extract and weigh information in each of three sources. These were (1) the scientific review literature, (2) experts in the fields of the medicine, toxicology, and epidemiology of reproductive and developmental toxicity, and (3) two national data bases. In developing the final list of 30, we relied heavily on our survey of experts as the most recent and most complete source of information on the status of knowledge about these chemicals in 1990.

purpose of our effort here was to ensure that in identifying the well-known chemicals, we did not go beyond scientific knowledge in the area.

Our work is based on two surveys: the first involved a sample of experts who played a prominent role in recent scientific conferences and workshops in the medicine, toxicology, and epidemiology of adverse reproductive and developmental outcomes (appendix I); the second queried officials working in the 10 federal offices previously mentioned. It is these officials who reported to us the information on their regulation of each of the chemicals on our list. We supplemented the two surveys with information from the published scientific literature, documentary analysis, and interviews with experts and officials in and out of government.

As already noted, we limited our study to nondrug environmental chemicals. Our intention was to include chemicals the public could be exposed to in the course of normal, legal life activities, such as working or smoking.[2] We do not directly assess the protection afforded by any particular federal regulation against reproductive or developmental toxicity. We relied instead on indicators such as agencies' judgments regarding their own regulations, expert judgments, and a critical examination of the

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[2]Thus industrial chemicals were candidates, but so were lithium and vitamin A which occur naturally. We decided to include alcohol and tobacco because they have a large impact and, yet, are often omitted from studies of both drugs and environmental exposures. We excluded illegal drugs.

agencies' regulatory decision-making process. Our data reflect regulatory actions the agencies reported to us as being in effect August 31, 1990.

Our study is thus intended to provide information on both the broad spectrum of chemical agents that pose reproductive and developmental hazards, and on the federal effort directed at their control. Although we focused on nondrug chemicals, proven toxicants include radiation, drugs, pesticides, industrial solvents, and naturally occurring elements and chemicals. The serious--indeed, frequently tragic--outcomes they produce suggest that they and other suspected reproductive and developmental hazards clearly deserve focused, systematic, and persistent regulatory consideration.

Federal Activity

Federal responsibility for protecting the public against environmental agents that cause disease is spread over many federal offices, but the entities that play the largest regulatory role are the Consumer Product Safety Commission, the Environmental Protection Agency, the Food and Drug Administration, and the Occupational Safety and Health Administration. Ten program offices in these four

agencies have responsibility for regulating environmental chemicals.[3] All 10 accept responsibility for protecting reproductive and developmental health. Those that do not have a specific mandate have interpreted their responsibility for reproductive and developmental disease under the general health and safety provisions of their legislation. Table 1 characterizes the office missions and mandates.

Table 1: Office Mission and Mandate to Protect Reproductive Health

Office	Mission	Legislation[a]	Mandate[b]
CPSC	Protect consumers from unreasonable risks of injury or illness from all household products	Consumer Product Safety Act	Yes
		Federal Hazardous Substances Act	No
		Poison Prevention Packaging Act	No
FDA/CFAN	Protect human health by regulating exposure to harmful chemicals in food, not chemicals per se	Federal Food, Drug, and Cosmetic Act	No
OSHA	Ensure safe and healthful working conditions	Occupational Safety and Health Act	No

[3]CPSC, FDA, and OSHA each have one office with primary responsibility for regulating environmental (nondrug) chemicals. EPA has seven offices with some regulatory responsibility for environmental chemicals. They are the Office of Air and Radiation (OAR), the Office of Drinking Water (ODW), the Office of Emergency and Remedial Response (OERR), the Office of Pesticide Programs (OPP), the Office of Solid Waste (OSW), the Office of Toxic Substances (OTS), and the Office of Water Regulations and Standards (OWRS). In a recent reorganization of the Office of Water at EPA, most of the functions of OWRS were transferred to the newly created Office of Science and Technology.

Table 1: Cont'd

Office	Mission	Legislation[a]	Mandate[b]
EPA/OAR	Protect and enhance the quality of the nation's air in order to promote the public health	Clean Air Act	Yes
EPA/ODW	Ensure safe drinking water supplies against contamination	Safe Drinking Water Act	No
EPA/OERR	Protect human health and the environment from threats by uncontrolled releases of hazardous substances	Comprehensive Environmental Response, Compensation, and Liability Act	Yes
EPA/OPP	Register pesticides ensuring no unreasonable risks to people or the environment and set legal limits for pesticides on food and feed crops	Federal Insecticide, Fungicide, and Rodenticide Act	No
		Federal Food, Drug, and Cosmetic Act	No
EPA/OSW	Ensure that hazardous waste management protects human health and the environment	Solid Waste Disposal Act	No
EPA/OTS	Protect public health and the environment from unreasonable risks posed by chemicals in commerce	Toxic Substances Control Act	Yes
EPA/OWRS	Restore and maintain the integrity of the nation's waters	Federal Water Pollution Control Act (Clean Water Act)	Yes

[a]Other federal laws provide for the regulation of toxic substances; however, they either deal with agencies or with types of hazards outside the scope of this study. In addition, these 10 offices have laws that are not relevant to our study.

[b]Indicates whether reproductive or developmental toxicity is specifically mentioned in the law.

The lack of scientific knowledge already discussed regarding reproductive and developmental toxicity presents a challenge to the development of a protective federal stance. Thus, a major obstacle to regulatory consideration of reproductive and developmental hazards is the lack of toxicity test information for most chemicals in commerce.

A second important obstacle to the regulation of reproductive and developmental hazards is the continued lack of a quantitative risk assessment protocol for these outcomes. For reproductive or developmental toxicity, as for all disease outcomes except cancer, agencies now use a less quantitative risk assessment protocol that does not allow the estimation of numbers of cases at risk. It also presumes there are low doses that pose no danger in contrast to the non-threshold assumption they make for cancer. Many scientists and agency staff as well are uncomfortable with the assumptions of the protocol used for reproductive and developmental toxicity. However, several proposals to refine risk assessment published over the last 6 years have yet to be implemented by EPA's program offices.

Findings

Question 1: Identifying Environmental Hazards of High Concern

No federal agency is required to publish a list of known human reproductive toxicants and no authoritative federal listing is

available for these diseases, such as the Annual Report on Carcinogens.[4] Despite this lack, we built on the efforts of state governments and individual researchers to develop a list of 30 widely acknowledged reproductive and developmental toxicants. The resulting list displayed here includes a full spectrum of chemical types and uses: naturally occurring metals and chemicals, various types of pesticides, solvents and other industrial chemicals, and several chemicals ingested in the course of personal habits, such as nicotine. Many of these chemicals have several different uses, and all have serious toxicities in addition to their reproductive and developmental consequences.

Alcohol	Ethylene dibromide	Nicotine
Arsenic	EGEE	PBBs
Cadmium	EGME	PCBs
Carbon disulfide	Ethylene oxide	2,4,5-T
Carbon monoxide	Gossypol	TCDD
Chlordecone	Hexachlorobenzene	Tobacco smoke
Chloroprene	Lead	Toluene
DDT	Lithium	Vinyl chloride
DBCP	Mercury	Vitamin A
DES	Mirex	Warfarin

Question 2: Extent of Regulation

The agencies reported taking 138 major regulatory actions on our list of 30 chemicals including (1) 20 cases of banning or canceling selected uses of the chemical, such as banning the

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[4]The 1978 amendments to the Community Mental Health Centers Act (P.L. 95-622) required that the Department of Health and Human Services prepare the Annual Report on Carcinogens, one part of which is to be a list of known or anticipated carcinogens to which a significant number of persons residing in the United States are exposed.

pesticide DDT, (2) 97 cases of setting numerical standards or restrictions on the chemical, such as setting maximum levels of arsenic allowed in drinking water, and (3) 21 cases of guidance or guidelines, such as the recommended allowable levels of mercury in fish. Since we asked the agencies to report only on the most significant regulation they took on each chemical; that is, "that with the greatest risk management impact," the set of actions represents the major federal structure of regulation for the chemicals we identified. However, it is not the total effort, as some offices may have taken multiple actions. The major regulatory activities reported to us are displayed in table 2.

The regulatory actions within this set represent a considerable range of activity frequently designed to mitigate disease resulting from environmental exposures. They make up a spectrum moving from complete control of a chemical via banning, through moderate control via standards, to weak control via guidelines. However, that impression may be misleading. A "ban," for example, does not necessarily mean that a chemical is comprehensively regulated or eliminated from the environment. DDT and Mirex are two banned pesticides on our list that are still manufactured in the United States. Several of the 20 "bans" are selective cancellations of particular uses. Arsenic pesticides were canceled for use on some agriculture products, whereas use is still approved on several other foods and in pressure-treated wood products.

Table 2: Major Federal Activities Reported for Chemicals of High Concern

Chemical	Type of Regulation			
	Guidance	Standard	Ban	Total
Alcohol		2		2
Arsenic	1	6	2	9
Cadmium	2	4	1	7
Carbon disulfide		4	1	5
Carbon monoxide		4		4
Chlordecone		2	1	3
Chloroprene		2		2
DDT	1	3	1	5
DBCP	1	3	1	5
DES		3	1	4
Ethylene dibromide	1	3	1	5
EGEE		4	1	5
EGME		1	1	2
Ethylene oxide		5		5
Gossypol		1		1
Hexachlorobenzene	2	2	1	5
Lead	1	6	2	9
Lithium		3		3
Mercury	2	5	1	8
Mirex	1		1	2
Nicotine		4		4
PBBs		1		1
PCBs	2	5	1	8
2,4,5-T	2	3	1	6
TCDD	2	4		6
Tobacco smoke				0
Toluene	2	5		7
Vinyl chloride	1	5	2	8
Vitamin A		2		2
Warfarin		5		5
Total	21	97	20	138

All but one of the 30 chemicals we identified are covered by one or more major regulatory actions. Two-thirds (20) of the chemicals are covered by at least four actions, and seven (toluene, vinyl chloride, PCBs, and the heavy metals lead, arsenic, mercury, and cadmium) were covered by seven or more actions. This degree of activity was not unexpected as most of these chemicals are acutely

toxic or carcinogenic in addition to having reproductive or developmental effects. Three-fourths of the decisions were made since 1980, but some of the earlier ones are 25 or more years old.

The actual hazard posed by the 30 chemicals depends on factors outside the scope of this study, such as the extent and magnitude of exposures. However, by using surrogate exposure indices frequently used by the agencies themselves, we have established that the presence of most of the 30 chemicals in our environment is likely. The indices we used are production volume and public concern. Public concern for many of the 30 chemicals is regularly and recently to be found in the national press. In our full report, we present U.S. production data for all but 4 of the 30 chemicals.[5] It is worth noting that even the 16 chemicals with one or more canceled pesticidal uses in this country may be manufactured or formulated here, or imported or exported. These chemicals are likely to occur in several media (for example air and water) and consequently fall under the regulatory domain of several offices.

Several of the 30 chemicals break down very slowly and as a consequence are "persistent" in the environment. As a result, exposures to DDT, PCBs, and hexachlorobenzene, for example, begin transplacentally before birth and continue through breast-feeding, and indeed throughout life.

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[5]Because some of these chemicals are "persistent" or naturally occurring, production is not the only source. Therefore, production figures are not total indicators of exposure.

Table 3 displays the actions reported to us in the six regulatory domains assigned by law to the 10 offices we reviewed. These domains are: water, toxics, air, consumer products, food, and work. Three domains (that is workplace, toxics, and water) have regulatory actions for more than 20 of our set of 30 chemicals. However, we found that for the domains of air and consumer products, fewer than 10 of the 30 chemicals had received any major regulatory action. Although it is difficult to draw conclusions regarding how much regulation is enough in a broad overview such as ours, we find the small amount of regulatory activity in these two domains problematic for 30 widely acknowledged reproductive and developmental hazards.

Take the case of toluene, for example. Toluene is a volatile chemical produced in large volume by American industry. The major exposures for this chemical are through vehicle emissions; indoor air from stored glue, paints and thinners; and occupational settings such as printing or paint manufacture. Water and food are unlikely to be major sources of toluene.

There are occupational studies and case reports showing that inhalation of toluene can lead to intrauterine growth retardation, developmental delay, and central nervous system dysfunction. In addition, some children were born with microcephaly and craniofacial

Table 3: The Extent of Regulation of Regulatory Domains for Chemicals of High Concern for Reproductive and Developmental Health[a]

Chemical	Domain					
	Water[b]	Toxics[c]	Air[d]	Consumer products[e]	Food[f]	Work[g]
Alcohol					X	X
Arsenic	XXX	X	X	X	X	X
Cadmium	XXX	X				X
Carbon disulfide	XX	X			X	X
Carbon monoxide			X	X	X	X
Chlordecone	XX	X				
Chloroprene	X					X
DDT	XX	X				X
DBCP	XX	X				X
DES	XX			X	X	
Ethylene dibromide	XX	X				X
EGEE	XX	X			X	X
EGME		X				X
Ethylene oxide	XX	X			X	X
Gossypol					X	
Hexachlorobenzene	XX	X				
Lead	XXX	X	X	X	X	X
Lithium				X	X	X
Mercury	XXX	X	X			X

(Continued)

Table 3: Cont'd

Chemical	Domain					
	Water[b]	Toxics[c]	Air[d]	Consumer products[e]	Food[f]	Work[g]
Mirex		X				
Nicotine	XX	X				X
PBBs		X				
PCBs	XX	XX			X	X
2,4,5-T	XX	X				X
TCDD	XX	X			X	
Tobacco smoke						
Toluene	XX			X	X	X
Vinyl chloride	XXX	X	X	X		X
Vitamin A				X	X	
Warfarin	XX	X		X		X

[a]The total number of bans and standards is 117. Multiple Xs indicate a major regulation from more than one office.

[b]The water domain regulations include those reported to us by the Office of Drinking Water, the Office of Water Regulations and Standards, Office of Solid Waste, and Office of Emergency and Remedial Response.

[c]The toxics domain regulations include those reported to us by the Office of Toxic Substances and by the Office of Pesticide Programs, which may have set limits on the amount of pesticides that can occur in food or specified labels for pesticides used as consumer products, although not necessarily for this list of 30 chemicals.

[d]The air domain regulations include only those reported to us by the Office of Air and Radiation.

[e]The consumer products domain include only those reported to us by CPSC.

[f]The food domain regulations include only those reported to us by the Center for Food Safety and Applied Nutrition.

[g]The workplace domain regulations include only those reported to us by OSHA.

and limb defects. Because of possible multiple solvent exposures, the occupational studies, like so many in this area, are not conclusive; however, animal tests that demonstrated toluene as a developmental toxicant at moderate levels, reinforce concern for adverse effects in man.

EPA's Office of Air and Radiation (OAR), the Consumer Product Safety Commission (CPSC), and the Occupational Safety and Health Administration (OSHA) would be the major lines of defense against the chief sources of exposure, since they are responsible for vehicle emissions, hazards from consumer products, and the health and safety of the workplace, respectively. However, after study, OAR declined to take action in 1984. The limited actions by CPSC to label and require childproof caps address child ingestion episodes, but not the concentrations of toluene in household air from stored products. OSHA did tighten its air standard for toluene in the workplace in 1989.

The adverse effects of alcohol and tobacco are perhaps the most widespread and preventable of any we discovered in our review. An estimated 10,000 infants are born each year in the United States with fetal alcohol syndrome, which produces a burden of mental retardation and disruptive behavior that affects every facet of their lives. We have strong evidence that tobacco smoke causes low birthweight and related problems. The Secretary of Health and Human Services

recently estimated that one-tenth of U.S. infant mortality is caused by mothers' smoking. Yet most of the 10 offices in our study find uncertain authority or are excluded by law from actively regulating the health effects of personal uses of alcohol and tobacco.[6] We found remarkably little regulatory activity from the 10 offices we reviewed on these two substances. At the very least, clarification of the legal responsibility of these 10 offices to regulate these chemicals seems indicated. Beyond that, it may be time to look carefully at the available data and consider more creative approaches to limiting exposures to these hazardous substances.

One encouraging example is that of lead. In recent months, lead has been singled out for an unusual cross-agency federal effort. The debilitating effects of lead on the developing nervous system from both prenatal and postnatal exposure are very serious, very well known, and certainly warrant such a concerted federal effort. However, treating lead as an exception, with different assumptions and protocols from the other chemicals on our list, may not be justified.

Question 3: Relationship of Regulations to Reproductive and Developmental Toxicity

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[6]They may regulate uses of alcohol and tobacco that are not personal. For example, OSHA has recently announced that they will consider regulating passive smoke exposure in work areas, a regulatory domain currently unregulated. OSHA noted that for smoke in certain public areas, such as shopping malls, EPA would be responsible.

For the set of 138 regulations that the offices reported to us as their actions with the greatest risk management impact, we found that regulation was most frequently based on diseases other than reproductive toxicity. Cancer and acute toxicity have played a large role, with cancer having been the sole basis or shared basis for 42 percent of the decisions. Just less than one-third of the regulatory decisions for the 30 chemicals were based, to any extent, on consideration of reproductive or developmental outcomes, although data for these toxicities may have been examined for a larger group (see appendix II). This pattern derives from the nature of the 30 chemicals with their multiple toxicities and the history of regulation in the United States, which has been predominantly focused on cancer and acute toxicity.

However, the pattern raises the issue of whether a set of regulations primarily based on other concerns can protect against reproductive or developmental toxicity. Although officials from each of the agencies attested that their policy is to base regulation on the "most sensitive disease endpoint"[6] and thus, protection would be ensured against all toxicities, their view is only partly reassuring. The issue here is how that endpoint has been selected. To protect against toxicity, it seems obvious that the proper identification of the "most sensitive disease endpoint" would first necessitate an examination of toxicity information for all endpoints. Instead, we found reproductive or developmental

[6]"Endpoint" here means the result of a toxic exposure.

information was not even examined in more than half the cases. Secondly, the different assumptions in risk assessment for different disease endpoints produces the artifact that cancer will very commonly be found to be "the most sensitive disease endpoint."[7] Finally, the nationally recognized experts in reproductive and developmental toxicity whom we surveyed expressed substantial reservations about the ability of cancer-based regulation, in particular, to protect against reproductive and developmental disease.

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[7]In brief, cancer risk assessment assumes that even small amounts of a carcinogen contribute to the development of the disease. This is a non-threshold disease model. Risk assessment as currently practiced in the federal government for all other diseases, including reproductive and developmental risk assessment, makes a threshold presumption. That presumption is that theoretically there is a dose level (the threshold) below which exposure does not contribute to disease progression. Federal risk assessment for reproductive and developmental diseases uses this threshold model to determine a reference dose calculated from levels discovered to have a proven effect, dividing by safety factors of 10 for human variation, the differences between animal and human sensitivity, etc. That is, the stringent practice of using conservative procedures to restrict cancer risk estimates to one in 100,000 or fewer, whereas procedures used to restrict teratogens allow much higher risks, result in the perception that cancer risks far exceed teratogenic risk for most chemicals.

There are several aspects of the current risk assessment approach that give us concern about its protective capacity. There are well-known reproductive and developmental hazards that act like non-threshold agents. In the cases of lead and radiation, no dose has been found to be without deleterious effect. One of the differences between cancer causation and reproductive and developmental toxicity is that for the latter, single peak exposures at critical times could produce an adverse reproductive or developmental event but may appear to be of little consequence in cancer risk assessment where cumulative doses over a lifetime are calculated.

To determine whether there was a pattern of association between offices that failed to use reproductive and developmental disease as a basis for regulations and a specific mention of reproductive or developmental health in their laws, we analyzed the offices' statutes. We found that only 5 of the 12 relevant laws mention reproductive or developmental disease, but there was no greater likelihood of offices with the more specific laws basing their regulations on reproductive or developmental disease than those with less specific laws. However, regulatory office respondents did, in some cases, perceive real or actual limits to their authority to regulate particular chemicals or classes of chemicals. We explore this subject in more detail in our report.[8]

In sum, we do not conclude that this set of regulations is, as a group, unprotective against all reproductive and developmental toxicities. In some cases, regulation based on one disease may protect against other toxicities. But because of the basis on which the regulations were decided (and especially the failure in more than half of the regulations to systematically examine data on reproductive and developmental toxicities) neither can we conclude that protection has been achieved.

Question 4: The Sufficiency of Regulatory Protection Against Reproductive and Developmental Disease

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[8]Reproductive and Developmental Toxicants: Regulatory Actions Provide Uncertain Protection (GAO/PEMD-92-3, October 1991).

A number of indicators taken together, do suggest that the set of major regulations in place against the 30 chemicals are, in fact, insufficiently protective against reproductive and developmental disease. First, as already noted, GAO found that agency decision-makers examined data on reproductive and developmental toxicities in fewer than half of the regulatory decisions. Several practices appear to have contributed to this pattern, including a lower priority for reproductive and developmental disease; limited or inaccessible reproductive data in an EPA data base; the as-yet undemonstrated assumption that regulation for other diseases protects against reproductive disease, and authority under law to adopt standards from nongovernment entities, which may not reflect a comprehensive health basis.[9]

Second, experts we surveyed in the spring of 1990 held a generally negative view of the protection offered by the current federal regulation of reproductive and developmental toxicants. Forty percent of the respondents judged the protection to be "fair," while another 38 percent judged it "poor to very poor."

Third, agency officials judged their own standards and guidelines to be of uncertain protection against reproductive disease in roughly half the cases. In our survey, we had asked the agency respondents to judge the protective value of each of the 138

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[9]We found 12 cases where standards were adopted from a nonfederal source without the examination of data, a situation apparently allowed under the law.

regulations against reproductive or developmental toxicity. The degree of confidence that offices placed in the protective nature of their own regulations varied by type of action and by office. They judged all bans protective. We have noted that with production, exports, and imports continuing, we are not as convinced of the protection a ban affords. But, on average, for the remaining 117 standards and guidelines, the agency respondents judged only 46 percent to be protective against reproductive or developmental disease. For the other 54 percent of cases, they indicated the regulation either did not protect or they were uncertain.

Fourth, in the absence of a quantitative risk assessment protocol for reproductive and developmental toxicity, it is difficult to claim that no risk exists, or even to establish what, if any, risk is left under a regulation aimed primarily against other diseases.

Fifth, one-quarter of the 138 major regulatory decisions were made before 1980. Many of these and also more recent decisions need revision either because they did not consider reproductive toxicity data available at the time or because new data have become available since then. For example, the Center for Food Safety and Applied Nutrition weakened its guideline for mercury in fish from 0.5 to 1 part per million in 1979 without examining data on mercury's reproductive toxicity. The original decision cited directly applicable evidence from the Minamata Bay, Japan, experience showing

the severe neurologic damage resulting to the children of mothers who ate fish contaminated with mercury. In revising the standard FDA reported they did not examine reproductive or developmental data. Instead they based the decision exclusively on neurotoxicity. Today, the Center is uncertain if that guideline protects against reproductive or developmental toxicity, and officials report that they are assessing the need to revise it.

Finally, a sizable portion of regulations the agencies judged not to be protective or to be of uncertain protection against these diseases are neither under revision nor under consideration for revision. Excluding bans, 42 percent of regulatory actions judged by agency officials not to be protective for reproduction or development and 67 percent judged to be of uncertain value are neither being revised nor being assessed for the need to revise.

Discussion and Summary

Overall, in spite of the agencies' general acceptance of responsibility for protection against reproductive and developmental disease and their testimony that they are on the forefront of the regulation of reproductive and developmental hazards, we found their policies and protocols have produced a pattern of second-class regulation for adverse reproductive and developmental outcomes. This pattern was clear, overall, for the 30 widely acknowledged hazards we reviewed and it is reasonable to presume it extends to the larger set

of reproductive and developmental hazards as well. Agencies do not list the chemicals they identify as reproductive hazards, nor do they consistently utilize the information available. This has resulted in more than half the chemicals we studied being regulated without examination of reproductive and developmental toxicity data. Even in the last 5 years, the rate of examination of these data in regulatory decisions for the 30 chemicals was only 55 percent. Our general conclusion is that, currently, the federal regulatory approach provides, at best, uncertain protection against reproductive and developmental toxicity.

Recommendations

Mr. Chairman, in a few weeks we will be issuing our full report for your Committee. Within that report we have a full array of recommendations based on our conclusions. Today, we simply want to highlight several.

We recommend that the Commissioners of CPSC, the Administrator of EPA, the Commissioner of FDA, and the Assistant Secretary of OSHA begin improving policies and practice by reviewing and revising the regulations for the 30 chemicals we reviewed and, in a reasonable time frame, extend the following improved practices to all future regulatory decision-making:

-- develop information on the occurrence of each chemical in the media, products, or situations of their responsibility;

-- conduct a search for and examination of the reproductive and developmental toxicity data for the unregulated chemicals proceeding to a thorough hazard assessment;

-- review the existing regulations on the 30 chemicals to determine whether they provide sufficient protection against reproductive diseases;

-- perform separate analysis for reproductive outcomes in risk assessments for these 30 chemicals and for future regulatory decision-making; and

-- ensure the ready availability of reproductive data to decisionmakers by asking the Congress for the power to demand reproductive toxicity test data from entities manufacturing, importing (including food imports), selling, emitting, or discarding reproductive hazards, and by organizing office data bases so that reproductive data are available.

Matters for Congressional Consideration

Congress might consider designating a federal office with the responsibility for preparing a periodic report which would list,

much as is done for carcinogens, the substances reasonably thought to be reproductive and developmental hazards to which a significant number of people in the United States are exposed. The same report should describe and evaluate regulatory actions on the substances. Such a listing effort at the federal level could stimulate regulatory attention to the problem and allow the public, responsible agencies, and the Congress to focus on chemicals for which action may be necessary.

The Congress could emphasize its concern for and focus agency attention on reproductive and developmental toxicity by amending those laws that do not currently specify the protection of the broad range of reproductive and developmental health and use of relevant toxicity data. The Congress could specify that all environmentally caused developmental, female reproductive, and male reproductive disease is part of the public health protection responsibility under the 12 laws.

We found that most of the 10 offices believe they do not have authority over various chemicals, and thus, alcohol, tobacco, and pesticides are less well regulated than they might otherwise be. In light of this, the Congress could consider making authority for alcohol and tobacco regulation explicit for the appropriate offices.

Considering that, in some cases, data may be absent or deficient, particularly in the case of chemicals beyond the 30 we

studied, the Congress might consider revising the laws to allow agencies to demand reproductive toxicity testing by the entities manufacturing, importing (including food imports), selling, emitting, or discarding products containing chemicals.

In light of our finding that one-quarter of the major regulatory decisions on the reproductive chemicals of high concern antedate 1980 and that a dozen standards adopted from nonfederal authorities are still the effective regulation or standard, the Congress should mandate that agencies establish a periodic review of regulations using recent information on reproductive and developmental toxicity. Specifically, the Congress might consider limiting the length of time regulations adopted from outside authorities can be maintained in lieu of federal decisions.

EXPERTS PARTICIPATING IN GAO SURVEY

We wish to thank the 50 scientists and administrators who responded to our survey. We have listed their names in alphabetical order, along with their affiliation.

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FEDERAL USE OF REPRODUCTIVE TOXICITY DATA

Overall, offices reported they did not examine reproductive or developmental data 55 percent of the time when they made the 138 major regulatory decisions, which casts doubt on the protective value against these outcomes of over half of the regulations. We expected a higher rate of examination of data because data are available on the list of 30 chemicals.[10] The several efforts to develop risk assessment protocols for reproductive toxicity assume that available data will be examined.[11] Finally, of the experts we surveyed, 98 percent indicated that reproductive or developmental data should "definitely" or "probably" be examined during risk assessment for chemicals that have multiple toxicities.

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[10]We found the data being utilized (1) by our published reviewers, (2) as entries in the national data bases, and (3) by our experts when they judged these chemicals to be of high concern.

[11]EPA, "Proposed Amendments for the Health Assessment of Suspect Developmental Toxicants, Request for Comments, Notice," 54 Fed. Reg. 42, Mar. 6, 1989, 9,385-403; "Proposed Guidelines for Assessing Female Reproductive Risk, Notice," and "Proposed Guidelines for Assessing Male Reproductive Risk and Request for Comments," 53 Fed. Reg. 126, June 30, 1988, 24,833-847, and 24,849-869. C.A. Kimmel, et al., "Overview of a Workshop on Quantitative Models for Developmental Toxicity Risk Assessment," Environmental Health Perspectives, 79 (1989), 209-15. B. Schwetz and R. Tyl, "Consensus Workshop on the Evaluation of Maternal and Developmental Toxicity Work Group III Report," Teratogenesis, Carcinogenesis, and Mutagenesis, 7 (1987), 221-327. D.M. Sheehan, et al., "Workshop on Risk Assessment in Reproductive and Developmental Toxicology: Addressing the Assumptions and Identifying the Research Needs," Regulatory Toxicology and Pharmacology, 10 (1989), 110-22.

Our analysis of the rates of data examination in major agency decisions reveals that, overall, the agencies increased their rate of examining reproductive data for decisions over time. As we would expect with data becoming more available, for this set of regulatory actions they examined data in only 10 percent of the cases before 1980 but in 66 percent of the cases between 1980 and 1984. The trend did not continue, but experienced some decline for decisions made since 1985--to only 55 percent of the cases.

Respondents gave three explanations for not examining data with approximately equal frequency: the mandate of the office did not require examining the data, the data were unavailable, and agency focus was not on reproductive and developmental toxicity. We found some evidence of policies that contribute to neglect of reproductive toxicity data, the assumption that regulation based on other diseases would probably protect against reproductive and developmental consequences, and an agency data base that makes access to reproductive and developmental data difficult.