United States General Accounting Office

GAO

Report to the Chairman, Committee on Agriculture, Nutrition, and Forestry, U.S. Senate

July 1993

PESTICIDES

A Comparative Study of Industrialized Nations' Regulatory Systems

149873

GAO/PEMD-93-17

GAO

United States
General Accounting Office
Washington, D.C. 20548

Program Evaluation and
Methodology Division

B-252075

July 30, 1993

The Honorable Patrick J. Leahy
Chairman, Committee on Agriculture,
Nutrition, and Forestry
United States Senate

Dear Mr. Chairman:

In response to your request, we are submitting this report, which discusses aspects of pesticide regulatory standards in Organization for Economic Cooperation and Development (OECD) nations. This report examines several issues related to establishing pesticide standards in these nations: data required for review before registering food-use pesticides, the organization and staffing of regulatory agencies, risk assessment and risk management procedures followed, and monitoring and enforcement measures in place. The report also discusses efforts to achieve greater harmonization of pesticide standards on the part of various international organizations. This information should assist the Committee in evaluating pesticide-related issues in their broader international context.

As agreed with your office, unless you publicly announce its contents earlier, we plan no further distribution of this report until 30 days from its date of issue. At that time, we will send copies to interested congressional committees and government agencies, and we will make copies available to others upon request.

If you have any questions or would like additional information, please call me at (202) 512-2900 or Kwai-Cheung Chan, Director of Program Evaluation in Physical Systems Areas, at (202) 512-3092. Major contributors to this report are listed in appendix III.

Sincerely yours,

Eleanor Chelimsky
Assistant Comptroller General

Executive Summary

Purpose

There has been increased public concern, both in the United States and abroad, about the potential health and environmental effects of pesticide use. Some of this concern is linked to expanding world agricultural trade and the movement of agricultural commodities among nations. The regulations that govern pesticide use have become issues of international importance, particularly in light of recent initiatives to harmonize them.

The Senate Committee on Agriculture, Nutrition, and Forestry is concerned about the effects that different national health and safety measures have on international trade. Senator Leahy, Chairman of the Committee, asked GAO to examine Organization for Economic Cooperation and Development (OECD) member nations' pesticide standards and regulations and compare them with those established in the United States. In discussions with Committee staff, GAO agreed to review the pesticide regulatory systems of the United States and OECD member nations along the following dimensions: (1) the types of experimental test data required to register food-use pesticides, (2) the organizational structures in place to evaluate pesticides, (3) the risk assessment and risk management procedures used, and (4) the measures employed to enforce pesticide standards.

Background

Most developed countries have established a regulatory process to determine the risks and benefits associated with pesticides and to promote their safe and effective use. Regulatory systems generally consist of laws and regulations that outline policies for the production, registration, and use of pesticides; mechanisms to evaluate product safety data and establish standards; and measures to monitor and enforce existing standards. There has been increased interest among OECD and European Economic Community (EEC) nations, and specifically within the administrative bodies of these two organizations, in harmonizing aspects of the pesticide regulatory process.

GAO used several different sources of data for this study. U.S. State Department staff stationed in each OECD country were asked to complete a survey that sought information on the pesticide standards in that country. Responses were received from 22 of the 24 OECD member nations. GAO also requested that State Department staff supply documentation describing pesticide registration data requirements; listings of these requirements were subsequently received for 18 OECD nations, as well as for the EEC. In addition, GAO staff visited Germany, Greece, Italy, Spain, and Sweden to

discuss pesticide regulation issues with government officials and representatives of other groups.

Results in Brief

GAO found a high degree of uniformity among OECD nations, including the United States, with regard to the kinds of test data that are required to register food-use pesticides. However, similar data requirements do not necessarily mean that countries receive the same information about a pesticide product or evaluate it in a similar manner. Important differences were found in data evaluation procedures, the transparency of the decision-making process, and the organization and staffing of agencies that regulate pesticides in the various OECD nations. For several evaluation procedures, such as those dealing with carcinogens, there is a divergence of scientific opinion concerning what approach is most appropriate. With regard to the level of technical resources and expertise available to conduct in-depth assessments of experimental test data, GAO found limitations in at least two of the OECD countries that were visited. Furthermore, the overall lack of written documentation in several OECD countries made it difficult to understand both their registration processes and their rationales for decisions concerning pesticides.

GAO found strong support for harmonization of pesticide regulations among the countries visited. The recent EEC initiative to harmonize the pesticide registration process will result in greater uniformity of test requirements and review procedures for member states. In addition, other efforts underway through the OECD and other organizations should strengthen cooperation among countries and improve information sharing about pesticide regulations. However, much work remains before regulatory differences among nations will be fully resolved.

Principal Findings

Data Registration Requirements

In reviewing the pesticide registration data requirements of 18 OECD nations and the EEC, GAO found a high level of agreement with U.S. requirements on the battery of toxicology tests used to assess human health effects of food-use pesticides. GAO found somewhat less agreement with regard to the tests that measure the impact of a pesticide on the environment and wildlife; these tests are less easy to standardize due to climatic and geological differences that are present across countries.

Countries also differ in the extent to which they have established formal test protocols. EPA, for example, has developed detailed guidelines that specify how tests should be conducted in the United States. Several OECD countries have not developed such guidelines but have indicated a willingness to accept test data generated according to the guidelines of OECD, EPA, or other international organizations. The EEC has also recently made considerable progress in developing specific guidance and procedures to structure the pesticide registration process in its member states.

Organizational Structures

The capability of a pesticide registration system to properly evaluate a chemical compound cannot be ascertained solely from its stated data requirements. In the course of conducting case studies in five selected OECD nations, GAO found important differences in the level of technical resources devoted to evaluating test data, as well as in the way each country structured the evaluation process. Greece, for example, had one full-time toxicologist and two other toxicologists serving in an advisory capacity. In contrast, EPA has found it necessary to build an organization of approximately 300 full-time staff representing different scientific disciplines devoted to evaluating registration petitions. Such differences in what countries require to execute their mission raise questions about the relative capabilities of nations to conduct scientifically sound reviews.

Evaluation Procedures

GAO found several differences in the data evaluation procedures used by OECD nations. For example, the United States uses what is termed a quantitative risk assessment model to estimate cancer risk, whereas OECD nations apply a threshold model. The best method of assessing cancer risks posed by pesticides is the subject of considerable debate, both in the United States and abroad, and work is being initiated to address differences in approach and methodology. In addition, unlike EPA, most OECD nations review data on product efficacy. This approach can promote safety by limiting the quantity of pesticides used. The United States, in contrast, places greater emphasis on market forces to minimize pesticide use, assuming that users will apply the minimum amount necessary of a pesticide. Further, the decision-making process leading to pesticide registration is often not made public in many OECD nations, thereby making it difficult to ascertain what other similarities and differences in evalution methods may exist.

Enforcement and Monitoring of Standards

GAO found that OECD nations' residue enforcement efforts generally focus on the testing of imported foods; less emphasis is given to exported products and domestically grown and consumed foodstuffs. The extent of monitoring efforts, however, varies among OECD countries. In some countries, testing has only recently been implemented, and in others available resources do not provide for comprehensive coverage of imports. Other countries have monitoring systems in place that routinely test food shipments.

GAO also found flexibility in the residue standards that OECD nations accept. For example, if a residue for which no national standard exists is detected on a food sample, OECD countries frequently consider Codex Alimentarius standards—a practice not followed by the United States.

Matters for Congressional Consideration

GAO found several fundamental differences across OECD nations' pesticide regulatory systems. Although at this time disparities across these nations appear to be too great to warrant taking what may be the final step in broader harmonization—recognition and acceptance of other nations' registration decisions—the Congress may wish to encourage EPA to conduct further work to clarify the extent and nature of these differences. The Congress may also wish to encourage EPA to expand its involvement in efforts to reach agreement on aspects of pesticide regulatory standards, as a way of furthering harmonization.

Agency Comments

Officials from the Department of Agriculture (USDA), EPA, and the Food and Drug Administration (FDA) reviewed a draft of this report and provided informal comments. Because of the nature of the report, the majority of the comments were made by EPA representatives. EPA officials believed that the report was essentially correct with respect to the technical and scientific matters discussed. They did make several technical observations, however, and these have been incorporated in the text where appropriate.

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Abbreviations

ADI	Acceptable daily intake
BBA	Biologische Bundesanstalt fur Land- und Forstwirtschaft (Germany's Biological Research Center for Agriculture and Forestry)
BBA-AP	Biologische Bundesanstalt fur Land- und Forstwirtschaft, Abtellung fur Pflanzenschutzmittel und Anwendungstechnik (BBA's Department for Plant Protection and Application Techniques)
BGA	Bundesgesundheitsamt (Germany's Federal Health Office)
CDC	Centers for Disease Control
EEC	European Economic Community
EPA	Environmental Protection Agency
FAO	Food and Agriculture Organization
FDA	Food and Drug Administration
FIFRA	Federal Insecticide, Fungicide, and Rodenticide Act
GAO	General Accounting Office
GATT	General Agreement on Tariffs and Trade
GIFAP	Groupement International des Associations Nationales de Fabricants de Produits Agrochimiques (International Group of National Associations of Manufacturers of Agrochemical Products)
IPCS	International Program on Chemical Safety
KemI	KemikalieInspektionen (Swedish Chemicals Inspectorate)
LC50	Lethal concentration (50)
LD50	Lethal dose (50)
MRL	Maximum residue limit
MTD	Maximum tolerated dose
NACA	National Agricultural Chemicals Association
NAFTA	North American Free Trade Agreement
NIH	National Institutes of Health
NTP	National Toxicology Program
OECD	Organization for Economic Cooperation and Development
OPP	Office of Pesticide Programs
PIC	Prior informed consent
RfD	Reference dose
UBA	Umweltbundesamt (Germany's Federal Environmental Office)
USDA	U.S. Department of Agriculture
WHO	World Health Organization

Introduction

Recent international efforts to reduce trade barriers, such as the Uruguay Round of the General Agreement on Tariffs and Trade (GATT), the North American Free Trade Agreement (NAFTA), and the movement within the European Economic Community (EEC) to establish a common market, have prompted increased interest in the equivalency of national product safety standards.

The issue of equivalency has been particularly troublesome in the area of agricultural trade because countries are reluctant to accept foreign commodities that have not met the same health and safety standards as domestic products. In 1990, the United States detained European wine shipments, a prominent example of a trade controversy created by dissimilar national health standards. At that time, the fungicide procymidone was legally authorized for use on wine grapes grown in several European countries; however, procymidone was not registered for use in, nor did it have a food tolerance established for, the United States. As a result, the wine was considered to be adulterated and, under the laws administered by the Food and Drug Administration (FDA), could not be permitted into this country. Although a temporary food tolerance for procymidone was later granted that allowed for the resumption of wine shipments, such regulatory actions on imported products, although reflecting genuine national concerns over health safety, can be interpreted as nontariff barriers to trade. If trade disruptions of this type are to be kept to a minimum in the future, it is important that countries achieve greater mutual understanding of the similarities and differences that exist among them with respect to health and safety standards. This report therefore focuses on the standards used to assess and regulate pesticides in the United States and other Organization for Economic Cooperation and Development (OECD) countries.[1]

Pesticide Regulatory Issues and Systems

Pesticides have become an integral component of agriculture throughout the world, contributing to increased yields and permitting new, more productive, cultivation techniques. In addition, pesticides play a critical role in disease prevention by controlling insects that carry malaria, yellow fever, typhus, and a host of other diseases. While past management is not exclusively limited to the use of synthetic compounds, they continue to be the most widely used means of controlling the majority of agricultural pests.

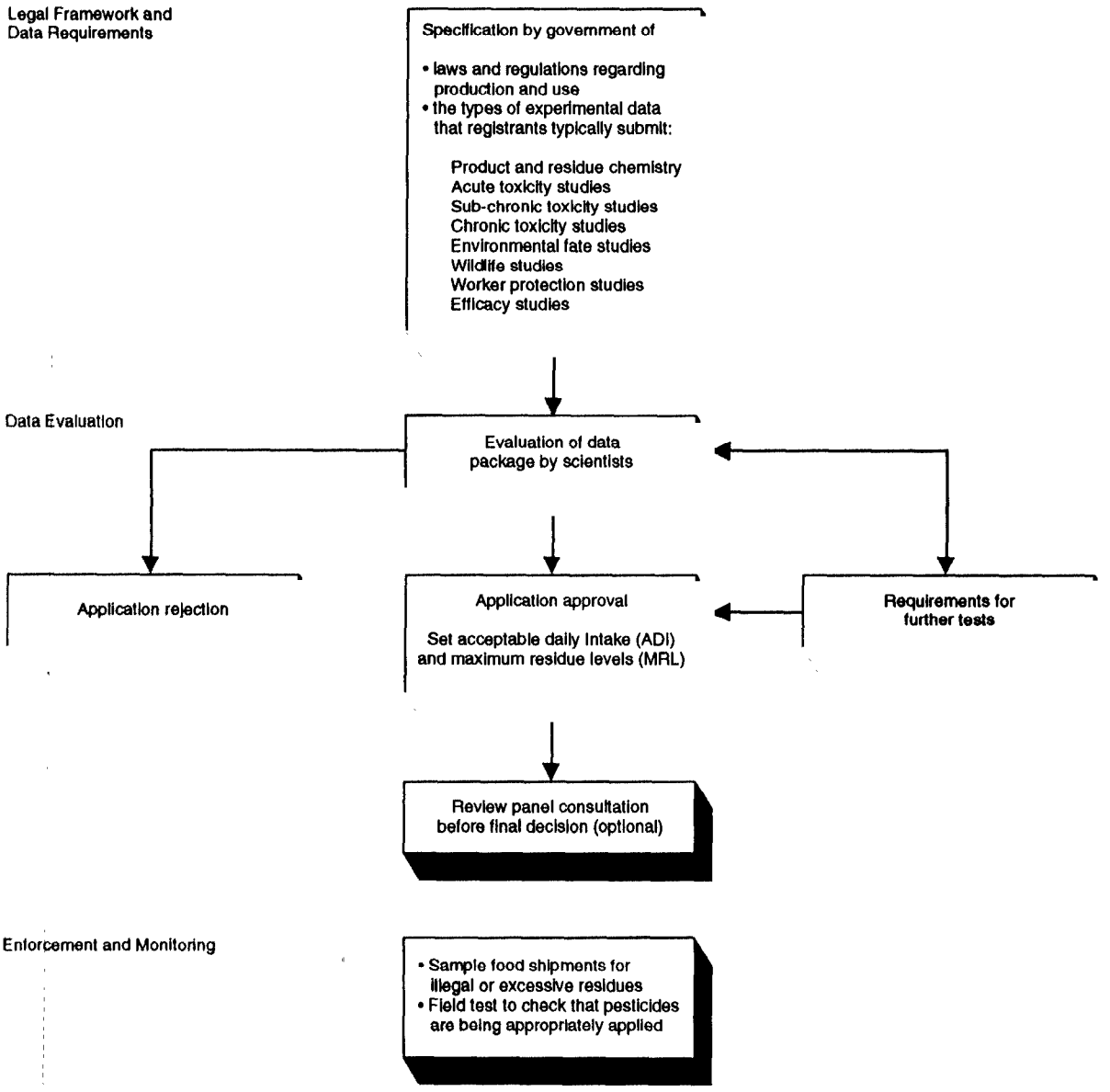
[1]The 24 OECD member nations are Australia, Austria, Belgium, Canada, Denmark, Finland, France, Germany, Greece, Iceland, Ireland, Italy, Japan, Luxembourg, the Netherlands, New Zealand, Norway, Portugal, Spain, Sweden, Switzerland, Turkey, the United Kingdom, and the United States.

Despite the beneficial aspects of pesticides, there has long been concern about their potential to adversely affect human health and the environment. In the early 1960's, concerns about pesticides focused on large-scale environmental problems associated with DDT and other insecticides that persist in the environment and cause dramatic problems for nontarget species. Further, the widespread presence of pesticide residues in the environment and on food means that at least some human exposure is inescapable.[2] This has raised concern over potential adverse health effects to humans stemming from long-term exposure.

Balancing the risks and benefits associated with pesticide use is the goal of the regulatory process. Figure 1.1 depicts in generic terms the three major components of pesticide regulatory systems: laws and regulations, a mechanism to evaluate product safety data, and measures to monitor and enforce pesticide regulations. As noted in the figure, a necessary precondition of a pesticide regulatory system is a body of laws and regulations that define administrative issues and policies related to the manufacture, labeling, approval, distribution, and use of these products. Regulations also stipulate the range of experimental test data that must be submitted for review in order to demonstrate a pesticide's safety. Test data are obtained by administering amounts of the compound to experimental animals; the results of these experiments are then used to extrapolate to humans those effects of a pesticide that are observed in the animals.

[2]See Scott R. Baker and Chris F. Wilkinson, eds., The Effects of Pesticides on Human Health (Princeton, N.J.: Princeton Scientific Publishing Company, 1990), p. 10.

Figure 1.1: Major Components of a Typical Pesticide Regulatory System



A second component found in most pesticide regulatory systems is a mechanism or structure to evaluate experimental test data and thereby

determine whether a compound poses health or environmental risks. These reviews are carried out by government scientists or consultants with expertise in toxicology, environmental ecology, or agricultural aspects of pesticide use. After examining test data submitted by the pesticide manufacturer, experts decide if the compound is safe for use. If it is, a food tolerance parameter is determined that specifies the maximum amount of pesticide residue—called a maximum residue limit (MRL)—permitted on food for human consumption (or in animal feed).

The enforcement apparatus that monitors pesticide use and enforces residue standards comprises the third component of a regulatory system. This includes monitoring residues on field crops, testing domestically grown and imported foods to determine whether tolerances are exceeded, and conducting studies of typical diets to determine the extent to which consumers are exposed to residues in foods.

Ensuring that chemical compounds used on agricultural crops do not pose an undue hazard to the public thus requires appropriate test requirements, procedures and personnel for evaluating test data, and an apparatus to ensure that pesticide regulations are enforced. If a regulatory system is deficient in any one of these areas, it may be ineffective in protecting public health or the environment.

Harmonizing Pesticide Registration Standards

Although the foregoing three components are present in the pesticide regulatory systems of most OECD countries, there are variations in the way each country organizes these efforts. During the past several years, an international movement to bring greater uniformity to the registration of pesticides has gained momentum with respect to both data requirements and the evaluation process. Leadership in the movement to "harmonize" pesticide registration has been taken by several organizations, notably the EEC, OECD, the Codex Alimentarius Commission, and the U.S. Environmental Protection Agency (EPA).[3]

[3]Other international organizations have also been active in related harmonization efforts. The Food and Agriculture Organization (FAO) has developed a series of guidelines related to pesticide control that cover legislation, registration, efficacy data, post-registration surveillance, and environmental criteria. FAO also shares operational responsibility with the United Nations Environment Program for overseeing the Prior Informed Consent (PIC) program. PIC is based on the principle that chemicals that are banned or severely restricted for health or environmental reasons should not be exported without the consent of relevant authorities in the recipient country. Efforts have also been under way since 1986 in the Uruguay Round of the General Agreement on Tariffs and Trade (GATT) to improve health-related regulations that affect agricultural trade.

While a variety of organizations have an interest in harmonization of pesticide standards, getting to that point is an evolving process with several objectives. At one level, harmonization could be viewed as acknowledging that different nations have reached broad consensus that consumer and environmental safety issues are being addressed. At another level, harmonization could be viewed as agreeing that different nations' data requirements and evaluation procedures are equivalent or nearly so, permitting the exchange and mutual acceptance of product reviews.

European Economic Community Registration Directive

The EEC has enacted legislation that will have important consequences for pesticide registration, reregistration of older products, and use in its member states.[4] In July 1991, the European Community Council of Ministers adopted a directive regulating plant protection products on the market throughout the EEC.[5] This directive has broad implications for the manner in which new and existing pesticides will be reviewed by EEC member countries, laying the groundwork for harmonization of pesticide registration. EEC member states are expected to comply with the directive by July 1993.

One of the major provisions of the directive specifies the establishment of uniform principles for data requirements and the evaluation of data in order to ensure that member states evaluate pesticides in an equivalent manner. A second provision calls for the mutual recognition of pesticide registration by nations in the EEC, provided that agricultural, plant health, and environmental conditions are comparable in the regions concerned.

A third change mandated by the directive is a shared review process whereby active ingredients currently on the market will, beginning in July 1993, be reregistered over a 12-year period on a proportional basis—which means that some countries will be assigned a greater number of pesticides to review than others—with 90 active ingredients scheduled for reevaluation in the first round of reviews. On the basis of these reviews, the EEC will develop a "positive list" of pesticides approved for use by member states.

[4]The 12 EEC states are Belgium, Denmark, France, Germany, Greece, Ireland, Italy, Luxembourg, the Netherlands, Portugal, Spain, and the United Kingdom.

[5]The directive, commonly referred to as 91/414/EEC, was published in the Official Journal of the European Communities, L (230/1), August 19, 1991, pp. 1-32.

OECD Initiative to Harmonize Pesticide Control Procedures

The OECD's Guidelines for Testing of Chemicals has been a standard reference volume since the late 1970's. These guidelines contain some 81 test protocols and are used by major pesticide manufacturers in preparing dossiers to register pesticides.[6] There has recently been interest in revising and updating the Guidelines for Testing of Chemicals to take into consideration new tests and other methodological advances that have occurred since the last update. OECD is working to update these test guidelines in 1993.

Toward this end, several international meetings have been held to discuss these issues. These meetings have been held in Sweden (October 1991), at the OECD offices in Paris (May 1992), in the United States (October 1992) and in Paris (March 1993). The meeting of OECD delegates held in May 1992, entitled "The Special Session on Pesticides," set the stage for subsequent work and focused on three key areas related to pesticide registration: common data requirements, revision of OECD test guidelines, and issues related to the evaluation and interpretation of data.

One issue under consideration by OECD member nations relates to the appropriate battery of test data that should be reviewed for registration purposes. The goal of this effort is to explore the extent to which it is possible to identify a set of "core" test requirements to properly evaluate a pesticidal compound.

Under this initiative, countries could still augment core test data with additional data requirements that address country-specific concerns—for example, those that measure a pesticide's impact on the environment or ecological conditions unique to a particular country.

Another issue being addressed by OECD relates to the process of evaluating and interpreting test data. The discussion at the May 1992 meeting revolved, in part, around the issue of the need for transparency in the procedures and criteria used to evaluate a pesticide. Procedural transparency refers to the ability of outside parties, in this case other OECD nations, to understand the rationale that a country used in making a registration decision. It has been suggested that transparency could be improved by having countries exchange written reviews of products that are produced by government agencies as part of the evaluation process.

[6]A companion volume, The OECD Principles of Good Laboratory Practice, was published in 1982 and updated in 1992. This publication outlines standard, high quality laboratory practices that can be used when conducting tests to support chemical registration applications. Both the Guidelines and Principles are published in Paris by OECD.

Such an effort has since been initiated through OECD and will initially focus on comparing different nations' reviews of seven pesticides.

The International Program on Chemical Safety (IPCS) is currently coordinating work in the health and environmental areas that could be useful in further standardizing pesticide reviews. There is interest in initiating work at IPCS on assessing carcinogenicity, with other projects related to assessment procedures to follow.[7]

Industry and Government Perspectives on Harmonization

Support for harmonization has come both from chemical manufacturers, who register and market their products throughout the world, and from government regulatory agencies. The agrochemical industry has backed the concept of harmonized test guidelines and data requirements as a way of reducing problems associated with what they view as different nations' duplicative and varying registration protocols. While manufacturers support harmonization as a way of reducing costs involved in preparing registration dossiers, they are also concerned that harmonization not result in the adoption of certain nations' most stringent regulatory requirements. Similarly, governmental agencies are interested in harmonization as a way of cutting administrative costs associated with data evaluation. At present, there is little intergovernmental collaboration in the evaluation of pesticides, and each agency must hire scientists or outside experts to evaluate test data that may already have received a thorough evaluation by scientists in other countries.

Despite the potential cost benefits of greater harmonization of registration standards, critics are concerned that the process not result in what could be termed the lowest common denominator —that is, the registration standards of the country with the least stringent standards emerge as the norm. Another concern about harmonization that has been raised is that data requirements and study protocols could become rigid and difficult to change as new scientific advances are made. This could particularly be an issue in nations where it is difficult to change government regulations.

[7]The International Program on Chemical Safety (IPCS) is a joint venture of the United Nations Environment Program, the International Labor Organization, and the World Health Organization (WHO). IPCS conducts and disseminates evaluations of how chemicals can influence the environment and human health. IPCS staff also develop different methods of assessing risk related to chemicals through laboratory, epidemiological, and related methods.

Regulatory Concerns Related to Registration Standards

In addition to reducing regulatory costs, the harmonization of registration standards may have potential to lessen the number of regulatory dilemmas of the type that sparked the recent congressional debate over the export of unregistered pesticides. Each year U.S.-based companies export large quantities of pesticides. While most U.S. pesticide exports are registered and approved for use in the United States by EPA, a number have either never been domestically reviewed or been banned from domestic use because of health or environmental concerns. Export of this class of products, permitted under current FIFRA legislation, has recently come under greater scrutiny.[8]

Legislation that would amend FIFRA and prohibit the export of unregistered and banned pesticides was introduced in the 102nd Congress by Senator Leahy (S. 898) and in the House by Representative Synar (H.R. 2083).[9] Supporters of both bills oppose the export of unregistered pesticides on human health, economic, or ethical grounds. There was agreement between the Bush administration and the Congress that export of banned pesticides should be prohibited because of the potential threat they could pose to human health. For other unregistered pesticides, there is concern that, because they have not been reviewed by EPA, they may pose potential hazards not only to foreign consumers but also to the American public because residues of these pesticides might be present on food imported into this country. Others have argued that the export of unregistered pesticides may hurt American farmers economically because foreign producers are able to use pesticides that are unavailable here. In addition, some have questioned the equity of exporting potentially hazardous pesticides that are not distributed domestically.

The Bush administration proposed several changes to existing FIFRA legislation during the debate over S. 898 and H.R. 2083. One amendment would permit the export of a pesticide with an unregistered active ingredient if it has been granted a U.S. food use tolerance, or if it is registered in an OECD member nation. Both EPA and some chemical industry representatives argue that OECD nations have processes for reviewing pesticides that are similar to EPA's. Moreover, EPA contends that OECD countries require essentially the same battery of experimental test

[8]FIFRA is the Federal Insecticide, Fungicide, and Rodenticide Act.

[9]This legislation is similar to a proposal adopted by the Senate and House during discussions surrounding the 1990 farm bill but removed during conference discussions.

data before granting registration as that required by EPA.[10] Accepting other countries' registration decisions—in this case, those made by OECD member nations—could provide the basis for the broader participation of the United States in efforts to harmonize pesticide registration standards.

Summary

Regulators will confront additional challenges as efforts to harmonize pesticide regulations gain momentum. An important element in this process will be the outlining of current registration requirements, and then finding agreement on the common set of requirements. Work under way by the EEC to harmonize data requirements for pesticide registration will certainly further this goal for member states. The OECD initiative to update its guidelines holds out the promise that consensus can be developed on core registration requirements potentially acceptable to a broader range of industrialized nations.

Objectives and Scope

Senator Leahy, Chairman of the Senate Committee on Agriculture, Nutrition, and Forestry, asked us to undertake a study of OECD member nations' pesticide standards and regulations, and to compare them to those established in the United States.[11] The request also asked that we review the procedures followed to establish these standards, how they are enforced, and the resources available for such enforcement. In discussions with Committee staff, we agreed on the following evaluation questions to guide our work:

1. What types of experimental test data do OECD member nations require to register food-use pesticides, and how do these requirements compare with those of the United States?

2. What organizational structures do OECD nations have in place to evaluate pesticides, and how do these structures compare with that of the United States?

3. What risk assessment and risk management procedures are used in OECD nations, and how do they compare with those of the United States?

[10]Other proposed amendments would prohibit the export of any pesticide banned or refused registration for human health reasons and also require pesticide manufacturers to develop residue detection methods for active ingredients exported but not registered in the United States.

[11]The present study builds upon an earlier report for the same committee that examined the comparability of U.S. and Codex pesticide regulatory standards. See International Food Safety: Comparison of U.S. and Codex Pesticide Standards, GAO/PEMD-91-22 (Washington, D.C.: August 22, 1991).

4. What measures are used to enforce pesticide standards in OECD nations, and how do they compare with those of the United States?

Methodology

This section discusses the methodology we developed for this study, beginning with a general overview of the methods we used and going on to more specific discussions that focus on each of our evaluation questions.

Interviews With Experts

To better understand current international pesticide registration issues, we conducted interviews with senior EPA, FDA, and U.S. Department of Agriculture (USDA) officials who occupy positions that bring them into contact with other nations' regulatory officials. In addition, we interviewed scientists and researchers who work for international organizations, consulting firms, and industry. We also reviewed relevant literature on this topic as part of our work.

Survey of State Department Staff

We then developed a survey that we sent to State Department employees stationed in OECD nations. The survey asked for registration guidelines and general information on pesticide regulatory issues. We received responses from 22 of 24 OECD nations, or 92 percent of those countries that were contacted.

Country Studies

To obtain more in-depth information on OECD nations' pesticide regulatory systems, we selected the following five OECD nations for country studies: German, Greece, Italy, Spain, and Sweden. We selected Germany because it is one of Europe's leading pesticide importers and exporters. Germany's data requirements, particularly those pertaining to the environment, are also believed to be in the forefront of European registration standards. Greece, Italy, and Spain were selected to provide a better understanding of pesticide regulations in southern European nations that export sizeable amounts of agricultural commodities to the United States. Of these three nations, Italy has the largest volume of agricultural exports to the United States. Greece and Spain also represent nations in which a relatively high proportion of the population is involved in agriculture. Sweden was selected because of the active effort on the part of its government to address pesticide use and control issues. To understand more about the international debate on harmonization, we also attended the Special Session on Pesticides that was held at the OECD offices in Paris in May 1992.

Prior to conducting country visits, we contacted staff working in their countries' Washington, D.C., embassies to obtain the names of agencies and staff responsible for pesticide regulatory efforts. While visiting these countries, we met with government officials and industry representatives, as well as persons working with international organizations (such as environmental groups) who were knowledgeable about pesticide issues. The goal of the country visits was to obtain a better understanding of these nations' regulations and registration data requirements, risk assessment and risk management procedures associated with pesticide approval, and enforcement capabilities and efforts.

In the following section, we briefly discuss the tasks we performed to answer each evaluation question.

Evaluation Question 1

To answer our first evaluation question—which asked about the types of experimental test data OECD member nations require to register a food-use pesticide and how these requirements compare with those of the United States—we requested a copy of each nation's registration guidelines as part of our survey of State Department staff. We received documentation on guidelines followed for pesticide registration from 18 nations, or 75 percent of OECD nations. Because 12 OECD member nations are part of the EEC, we also obtained and reviewed appropriate EEC directives relevant to pesticide registration. A summary of these guidelines is presented in matrix form in chapter 2. The matrix was developed using the 1991 edition of the Code of Federal Regulations. (Our coding procedures are discussed in appendix I.)

Evaluation Question 2

Our second evaluation question asked how the organizational structures employed by OECD nations to evaluate pesticides compare with that of the United States. We addressed this question by conducting country visits, reviewing relevant literature, and attending international meetings where this issue was discussed. We also asked several questions in our survey that focused on the scope of pesticide registration and reregistration efforts conducted by OECD nations during 1991.

Evaluation Question 3

Our third evaluation question asked how the risk assessment and risk management procedures used in OECD nations compare with those of the United States. We collected most of the information used to answer this question through interviews conducted during country visits. We were also

able to learn more about this topic by attending international meetings and interviewing experts.

Evaluation Question 4

Our fourth evaluation question asked how the measures that are used to enforce pesticide standards in OECD nations compare with those in place in the United States. We addressed this question through the survey, which asked about enforcement methods used, types of shipments targeted, and whether international standards are accepted if no national standard exists. We supplemented these data with information we collected on country visits.

Table 1.1 summarizes our data collection methods and the issues we address in this report. We conducted our work between January and October of 1992. We visited countries in May and June and requested information from embassies and other sources, such as EPA, between January and May 1992.

Table 1.1: Evaluation Questions and Data Collection Methods

Evaluation question	Issue	Data collection methods
Question 1	Compare test data requirements of OECD countries	Survey of registration guidelines of 18 OECD countries
Question 2	Compare organizational structure of agencies that evaluate pesticides in selected OECD counties	Country visits, review of relevant literature, international conferences, and survey of U.S. embassy staff
Question 3	Compare risk assessment and risk management procedures in selected OECD countries	Interviews with experts, review of relevant literature, country visits
Question 4	Assess enforcement measures	Country visits and survey of U.S. embassy staff

Study Strengths and Limitations

Strengths

To date, little information has been systematically collected on international pesticide registration requirements. Our study brings together information about many different systems, reviewing 18 OECD nations' registration requirements and those of the EEC. The matrices we prepared and our analyses of these requirements provide an overview of

these nations' toxicological and environmental test requirements. In addition, this study should by useful in informing the debate concerning the extent to which there is international agreement on standards and should also contribute to discussions about where there is agreement (and disagreement) in registration requirements, risk assessment and risk management procedures, and enforcement measures.

Limitations

Although this report can contribute to discussions about the issues outlined in the previous section, there are certain aspects of these discussions that are sufficiently complex that resolving them will require both time and the best efforts of scientists in many countries. For example, with regard to the data required to register a pesticide, there are nuances concerning test protocols and experimental design that may need to be looked at closely before agreement can be reached on what constitutes comparable standards.

Similarly, while we examined several important issues concerning the procedures used to evaluate pesticides in OECD countries, our analysis is best used for comparative purposes, as a way of highlighting areas of significant agreement or disagreement. It was beyond the scope of our work to judge the scientific soundness of decisions made on the basis of these procedures.

Organization of This Report

In chapter 2, we analyze the registration requirements of 18 nations and the EEC in matrix form, highlighting similarities and differences in tests required for registration. Chapter 3 contains an analysis of the organizational structures of five OECD nations where we conducted country visits. In chapter 4, we summarize differences in risk assessment and risk management procedures, as well as the philosophies that guide pesticide regulatory efforts in case study nations. Chapter 5 contains a discussion of how pesticide standards are enforced and monitored in OECD nations. In chapter 6, we present conclusions and matters for congressional consideration.

Appendix I describes the methodology used to code registration materials, the results of which are given in chapter 2. Appendix II contains summary data on 17 unregistered pesticides produced in, and exported from, the United States, as well as a description of the data collection instrument we asked chemical manufacturers to complete.

Data Required for Registering Pesticides in OECD Member Nations

Introduction

In this chapter, we answer our first evaluation question, "What types of experimental test data do OECD nations require to register food-use pesticides, and how do these requirements compare with those of the United States?" To support the registration of a pesticide, manufacturers are typically required to generate and submit a wide range of data that describe the pesticide's physical properties, chemical composition, and how well it performs, as well as identify any potential human health and environmental risks associated with its use.[1] The main focus of this chapter is on describing the toxicological and environmental data requirements. Using documentation provided by 18 of the 24 OECD countries and the EEC, we also compare the range of toxicology and environmental/wildlife tests required to register a pesticide in the United States with the corresponding standards of other OECD member nations.[2] We also briefly discuss a recent OECD study on this same topic.

Registration Documentation

Documentation on the kinds of test data required to register a pesticide in individual countries is prepared for registrants by the governmental agency or agencies responsible for pesticide registration. In addition to listing test data requirements, registration packets commonly include information on the licensing fees, procedures for submitting data, and acceptable test protocols, as well as other miscellaneous information.

Coding Format for OECD Country Guidelines

We used EPA standards as a point of reference in classifying the test requirements described in the registration materials received from other OECD countries. In coding these materials, we followed part 158 of Title 40 of the Code of Federal Regulations, 1991 edition, which presents, in summary form, the battery of test data required to register a pesticide in the United States. This classification format does not encompass all possible toxicological tests. Some tests mentioned in the guidelines of certain OECD countries are not included in the list of U.S. data requirements; for example, Germany and several other European

[1]For compounds that are chemically similar, manufacturers can utilize data previously submitted for other product registrations, including those obtained by other manufacturers. Because test data generated by private parties are considered proprietary, manufacturers seeking to register a product under EPA's "me too" provision must obtain permission to use such data from the party that originally generated it.

[2]State Department staff were not able to provide us with information on the data requirements for registering a pesticide in the following countries: Iceland, Ireland, Luxembourg, New Zealand, Switzerland, and Turkey. Icelandic officials indicated that while no published guidelines were available, the Ministry of Health and Social Security was drafting regulations for setting food safety standards. Officials from New Zealand stated that they use standards developed by the World Health Organization (WHO). We obtained a copy of these standards, but they lacked the requisite specificity to be coded here.

countries require data on a pesticide's impact on earthworms—a test not required by EPA. U.S. standards are very extensive, however, and include a broad variety of possible test requirements. By using U.S. standards to organize the coding of registration materials from other countries, we are able to address directly the question of how OECD nations' data requirements compare with those of the United States. (See appendix I for a complete description of the methodology used to code data requirements.)

Analysis of OECD Data Requirements

For the purposes of this report, we have organized the basic data requirements for food-use pesticides into three broad categories: (1) toxicological tests (divided into three subsections: acute, subchronic, and chronic); (2) ecological tests (divided into two subsections: environmental fate and wildlife tests); and (3) other tests (product chemistry, efficacy, reentry protection effects).[3] Because of their salience to human health concerns, we have included a brief description of each of the required tests in the following country-by-country comparison of toxicology data requirements. More extensive definitions, as well as those pertaining to the other data requirements, can be found in the various subdivisions of EPA's Pesticide Assessment Guidelines.

Toxicology Data Requirements

Acute Toxicology Studies

Acute studies are performed early in the testing process. As noted in the Code of Federal Regulations, they provide information on health hazards likely to arise soon after, and as a result of, short-term exposure. The information obtained from acute tests is used to construct precautionary labels for products, establish appropriate dose levels for subchronic and other tests, and identify potential health hazards to eyes and skin.

Table 2.1 shows that there is near unanimity among OECD countries with respect to acute toxicology data requirements, the one exception being the acute delayed neurotoxicity test that only five countries included in their acute toxicology regimen.

[3]In addition to pesticides intended for use on food crops, the Code of Federal Regulations also specifies the data requirements for registering a wide assortment of nonfood-use pesticides. These include treatments for tobacco, ornamental plants, animal feed, household insects, termites, swimming pools, and domestic animals. Because the data requirements pertaining to food-use pesticides are the most extensive and relevant to human health concerns, they were selected as the basis of our country-by-country comparison. It should be noted that other nations may exercise more stringent control than does the United States over pesticides that have domestic or ornamental uses.

Table 2.1: Acute Toxicology Data Requirements[a]

	Acute tests						
Country	Oral toxicity	Dermal toxicity	Inhalation toxicity	Eye irritation	Dermal irritation	Dermal sensitization	Acute delayed neurotoxicity
Australia	•	•	•	•	•	•	
Austria	•	•	•	•	•	•	
Belgium	•	•	•	•	•	•	
Canada	•	•	•	•	•	•	•
Denmark	•	•	•	•	•	•	
Finland	•	•	•	•	•		
France	•	•	•	•	•	•	
Germany	•	•	•	•	•	•	
Greece	•	•	•	•	•	•	
Italy	•	•	•	•	•	•	•
Japan	•	•	•	•	•	•	•
Netherlands	•	•	•	•	•		
Norway	•	•	•	•	•	•	
Portugal	•	•	•	•	•	•	•
Spain	•	•	•	•	•		
Sweden	•	•	•	•	•	•	
United Kingdom	•	•	•	•	•	•	•
EEC	•	•	•	•	•	•	•
United States	b	b	b	b	b	b	b

[a]Cells that contain a "bullet" signify that a test was listed in a country's published data requirements. While this code suggests general equivalence between foreign and U.S. standards, it does not imply that the foreign requirement is identical to the corresponding standard listed in the Code of Federal Regulations. In most instances, the registration guidelines we reviewed did not provide sufficient specificity for us to make that determination. Empty cells indicate that a specific test was not cited in a country's registration documentation and thus imply that the test is not required for registration.

[b]Test is required.

- The acute oral toxicity test provides information on health hazards likely to arise from short-term oral exposure and is traditionally used to establish a dose regimen for subchronic and other studies.
- The acute dermal toxicity test assesses the adverse effects on the skin during or following a single dose of a test substance.
- The acute inhalation toxicity test assesses the total adverse effects caused by a single uninterrupted exposure by inhalation.

- The eye irritation test assesses effects on the eye at two levels: "eye corrosion" (that is, irreversible tissue damage) and "eye irritation" (that is, reversible changes in the eye).
- The dermal irritation test assesses the adverse effects on the skin at two levels: "dermal corrosion" and "dermal irritation."
- The dermal sensitization test assesses an immunologically-mediated cutaneous reaction to a substance.
- The acute delayed neurotoxicity test measures prolonged delayed-onset locomotor ataxia—that is, the inability to coordinate voluntary muscular movements.

In the United States, the acute delayed neurotoxicity test usually required for organophosphorus compounds serves as a screening mechanism. If results from this test suggest that a compound has the potential to cause neurological problems, EPA may ask for additional studies. It should be noted that, although the use of this acute test was not widespread, the majority of the OECD countries we reviewed required some form of long-term neurotoxicity testing.

One acute toxicology test found in the requirements of several OECD countries (but not required by the United States) involves administering the test substance through an intraperitoneal route. This acute test entails placing the test substance directly into the abdominal cavity of the laboratory animal by means of injection.

Subchronic Studies

Subchronic studies provide information on health hazards that may arise from repeated exposure to a pesticide over a limited period of time (usually 3 months in animal tests), depending on the potential exposure to a pesticide. Subchronic test data are typically used to select dose levels for long-term (chronic) studies and to help establish criteria for human exposure.

All OECD countries in our sample required some form of subchronic testing. In contrast to the series of acute tests, however, the subchronic tests required exhibited less uniformity. While subchronic feeding studies were commonly required, at least one third of OECD countries did not require either a subchronic inhalation study or a subchronic dermal exposure study. (See table 2.2.) It should be noted that "subchronic" observations can be made in the course of longer-term chronic studies, thus fulfilling requirements for both types of test. Consequently, the absence of this requirement does not necessarily mean that registrants do not submit some type of subchronic data to these nations.

Table 2.2: Subchronic Data Requirements[a]

	Subchronic tests				
Country	90-day feeding study: rodent	90-day feeding study: non-rodent	Dermal study	Inhalation study	Neurotoxicity study
Australia	•	•	•	•	
Austria	•	•	•	•	•
Belgium					•
Canada	•	•	•	•	•
Denmark	•	•			•
Finland	•	•			
France	•	•	•	•	•
Germany	•	•			
Greece	•	•	•	•	•
Italy	•		•	•	•
Japan	•	•	•	•	•
Netherlands	•	•	•	•	•
Norway	•	•			•
Portugal	•	•	•	•	•
Spain	•	•	•	•	•
Sweden	•	•			•
United Kingdom	•	•		•	•
EEC	•	•	•	•	•
United States	[c]	[c]	[d]	[d]	[d]

[a]Cells that contain a "bullet" signify that a test was listed in a country's published data requirements. While this code suggests general equivalence between foreign and U.S. standards, it does not imply that the foreign requirement is identical to the corresponding standard listed in the Code of Federal Regulations. In most instances, the registration guidelines we reviewed did not provide sufficient specificity for us to make that determination. Empty cells indicate that a specific test was not cited in a country's registration documentation and thus imply that the test is not required for registration.

[b]The guidelines of most OECD countries list "neurotoxicity studies" under the heading of "chronic studies."

[c]Test is required.

[d]Test is conditionally required.

- The 90-day feeding study: rodent assesses the adverse effects occurring as a result of the repeated daily oral dosing of experimental animals with a chemical for approximately 10 percent of their life span.

- The 90-day feeding study: non-rodent measures adverse effects on non-rodents. (See preceding definition.)
- The dermal study provides information on possible health hazards likely to arise from repeated skin exposure.
- The inhalation study determines the no-observed-adverse-effect level (that is, dosage) and toxic effects associated with repeated exposure to a test substance for a period of 90 days.
- The neurotoxicity study measures prolonged delayed-onset locomotor ataxia—that is, the inability to coordinate voluntary muscular movements. Multiple doses of the test substance are administered over 90 days.

Chronic and Special Toxicology Studies

EPA guidelines state: "The objective of a chronic toxicity study is to determine the effects of a substance in a mammalian species following prolonged and repeated exposure....Ideally, the design and conduct should allow for the detection of general toxicity including neurological, physiological, biochemical, and hematological effects and exposure-related morphological (pathology) effects."[4] Thus, in contrast to acute toxicology tests that attempt to detect immediate health hazards, and subchronic tests that attempt to detect health hazards over a short period of exposure, chronic tests attempt to determine what, if any, long-term consequences are associated with exposure to a pesticide. These studies are typically conducted over a 2- to 4-year period. Long-term hazards include cancer, infertility and reproductive abnormalities, and dysfunctions of vital organs.

Chronic hazard testing was required by all countries for which we received guidelines. Moreover, the types of chronic studies required by OECD countries closely paralleled U.S. standards. With few exceptions, the OECD registration guidelines we reviewed called for studies in each of the five major groups of chronic tests. (See table 2.3.) However, despite agreement concerning the general kinds of chronic data that should be submitted to register a pesticide, many country guidelines were indeterminate with respect to certain aspects of experimental protocol. For example, U.S. standards require that two mammalian species be used when conducting chronic feeding, oncogenicity, and teratogenicity studies. In their registration materials, many other OECD countries did not explicitly specify that two species be used for this series of chronic tests. This difference may reflect a broader debate about how such tests should be conducted and what constitutes the correct test protocol.

[4]EPA, Pesticide Assessment Guidelines, Subdivision F (Washington, D.C.: 1984), p. 107.

Table 2.3: Chronic and Special-Requirement Tests[a]

	Chronic tests					Special requirement tests		
Country	Feeding study	Oncogenicity	Teratogenicity	Reproduction	Mutagenicity	General metabolism	Dermal penetration	Domestic animal safety
Australia	•	•	•	•	•	•	•	•
Austria	•	•	•	•	•	•		
Belgium	•	•	•	•	•	•		
Canada	•	•	•	•	•	•	•	
Denmark	•	•	•	•	•	•		
Finland	•	•	•	•	•	•		
France	•	•	•	•	•	•		•
Germany	•	•	•	•	•	•		•
Greece	•	•	•		•	•		
Italy	•	•	•	•	•	•		•
Japan	•	•	•	•	•	•		
Netherlands	•	•	•	•	•	•		
Norway	•	•	•	•	•	•		
Portugal	•	•	•	•	•	•		•
Spain	•	•	•	•	•	•		
Sweden	•	•	•	•	•	•		
United Kingdom	•	•	•	•	•	•	•	
EEC	•	•	•	•	•	•	•	•
United States	b	b	b	b	b	b	c	c

[a]Cells that contain a "bullet" signify that a test was listed in a country's published data requirements. While this code suggests general equivalence between foreign and U.S. standards, it does not imply that the foreign requirement is identical to the corresponding standard listed in the Code of Federal Regulations. In most instances, the registration guidelines we reviewed did not provide sufficient specificity for us to make that determination. Empty cells indicate that a specific test was not cited in a country's registration documentation and thus imply that the test is not required for registration.

[b]Test is required.

[c]Test is conditionally required.

- The feeding study is often combined with an oncogenicity study and performed to determine the effects of a substance in mammalian species (rat and mouse). This test is used to determine the potential oncogenicity (that is, tumor formation) and general toxicity (neurological, physiological, biochemical, hematological).
- The oncogenicity study (see preceding description).

- The reproduction study provides general information concerning the effects of a test substance on reproductive functions.
- The teratogenicity study measures the potential of a test substance to induce structural and/or other abnormalities into the fetus.
- The mutagenicity study measures the potential of a substance to affect the integrity of the mammalian cell's genetic components. The United States requires a representative selection of tests from the following three categories: (1) gene mutation; (2) structural chromosome aberration; and (3) other genotoxic effects (for example, DNA damage and repair, and numerical chromosomal aberrations).
- The metabolism study determines or characterizes the amount and rate of absorption, the pattern of distribution among tissues and organs, routes of excretion, and any possible bioaccumulation.

OECD countries also appear to differ from the United States in the way they structure the mutagenicity test requirement. While U.S. standards specify a range of specific mutagenetic tests that are acceptable, the battery of submitted data must include tests in each of three primary areas: (1) gene mutation, (2) structural chromosome aberration, and (3) other genotoxic effects. We did not find this particular type of test configuration in the data requirements of other OECD countries, although they all required some form of mutagenicity testing.

With regard to "special requirement test" data, we found that all of the country guidelines we reviewed required a general metabolism study. Conversely, only three countries (Canada, Australia, and the United Kingdom) and the EEC requested a dermal penetration study, while five nations and the EEC requested a domestic animal safety study as part of their toxicology regimen. The absence of the latter two types of studies from the list of requirements of most OECD countries may be explained, in part, by the function served by these tests. Metabolism studies address a broad range of concerns and the data generated from them directly complement chronic feeding and oncogenicity studies. Dermal penetration and domestic animal safety studies, on the other hand, are both conditionally required by EPA. The data generated by such studies are intended to address safety concerns raised by earlier tests or as a result of the product's having atypical use patterns; hence, definitive experimental protocols cannot be specified in advance. In lieu of explicit test guidelines for dermal penetration studies, EPA recommends that registrants "work closely with the Agency in developing acceptable protocols."[5] Thus, the conditional character of these requirements, as applied in the United States, may explain why neither dermal penetration nor domestic animal

[5]40 C.F.R. sec. 158.202 (1991).

safety test studies appear in the registration guidelines of other OECD countries.

Ecological Studies

Environmental Fate

The ideal pesticide would serve its intended purpose by eradicating the target pest without leaving a trace or residue. In practice, however, some pesticides have chemical properties that cause them to persist in the soil for many years, migrate into adjacent localities, or leach into the groundwater supply. Environmental fate studies are an attempt to gauge such properties. Data generated by these studies are used to determine the health risk to humans arising from exposure to pesticide "residues remaining after application, either upon reentering treated areas or from consuming inadvertently-contaminated food."[6] In addition, environmental fate test data are useful for estimating the potential environmental impact of pesticides on wildlife and nontarget organisms.

As table 2.4 demonstrates, the registration guidelines of most OECD countries require some form of environmental fate testing. With regard to specific tests, OECD countries list many of the same types of environmental fate tests that are required in the United States. Seventeen of the 18 countries for which we have data require a degradation study, 9 an accumulation study, and 16 a mobility study. Thirteen nations require dissipation field studies, and 7 nations require metabolism studies conducted in the lab. We note that EPA revised its environmental fate and ecological effects requirements in October 1992, thus reducing the number of "required" studies. Those changes are not reflected in tables 2.4 through 2.6.

[6]40 C.F.R. sec. 158.202 (1991).

Table 2.4: Environmental Fate Data Requirements[a]

	Chronic tests				
Country	Degradation studies	Metabolism studies: lab	Mobility studies	Dissipation studies: field	Accumulation studies
Australia	•	•	•	•	•
Austria	•	•	•	•	
Belgium	•		•		
Canada	•	•	•	•	•
Denmark	•	•	•	•	•
Finland	•		•	•	•
France	•		•	•	
Germany	•	•	•	•	•
Greece	•		•	•	
Italy	•		•	•	
Japan					
Netherlands	•		•		•
Norway	•		•	•	•
Portugal	•	•	•	•	•
Spain	•		•	•	
Sweden	•	•	•	•	•
United Kingdom	•				
EEC	•	•	•	•	•
United States	b	b	b	b	c

[a]Cells that contain a "bullet" signify that a test was listed in a country's published data requirements. While this code suggests general equivalence between foreign and U.S. standards, it does not imply that the foreign requirement is identical to the corresponding standard listed in the Code of Federal Regulations. In most instances, the registration guidelines we reviewed did not provide sufficient specificity for us to make that determination. Empty cells indicate that a specific test was not cited in a country's registration documentation and thus imply that the test is not required for registration.

[b]Test is required.

[c]Test is conditionally required.

Wildlife, Aquatic Organisms, and Nontarget Species

The data requirements pertaining to wildlife, aquatic organisms, and nontarget species, commonly referred to as ecotoxicity studies, are intended to estimate potential hazards to nontarget birds, wild mammals, fish, aquatic invertebrates, and pollinators (honeybees). In a natural setting, a wide variety of species are likely to be exposed to pesticide residues. Since it is impractical to study all species likely to be affected, some limits on testing must necessarily be imposed. As noted earlier in

this chapter, choosing the appropriate species and test dosage for a wildlife study may be problematic.[7] EPA wildlife data requirements are focused on assessing the impact of pesticides on wild birds and fish. EPA recommends that, in conducting these studies, mallards or bobwhites be used in studies involving birds and that rainbow trout or bluegills be used for fish studies.

We found the battery of data requirements pertaining to wildlife and insects to be the areas of least agreement among OECD countries, which perhaps reflects the difficulty of selecting the most ecologically salient test species. (See tables 2.5 and 2.6.) While all the guidelines we analyzed indicated that wildlife tests were required to register a pesticide, this requirement was often couched in very general terms.

[7]EPA recommends that avian test species should (1) demonstrate sensitivity to the effects produced by known toxic chemicals; (2) be ecologically significant—that is, occur naturally in large numbers and in widespread habitats; (3) be aesthetically or economically valuable to man; (4) be readily available for test purposes and not be an endangered or threatened species; and (5) have characteristics that will reveal observable effects (caused by a pesticide) within a reasonable period of time. See EPA, Pesticide Assessment Guidelines, Subdivision E (Washington, D.C.: 1982), pp. 9-11.

Table 2.5: Matrix of Wildlife Data Requirements[a]

Country	Avian oral: LD50	Avian dietary: LC50	Wild mammal toxicity	Avian reproduction
Australia	•	•	•	•
Austria	•			•
Belgium	•	•		
Canada	•	•		•
Denmark		•		•
Finland	•			
France	•	•		•
Germany	•	•	•	
Greece				
Italy	•	•		•
Japan				
Netherlands	•			
Norway	•	•	•	
Portugal	•	•	•	•
Spain	•	•		
Sweden	•	•		
United Kingdom	•	•	•	•
EEC	•	•	•	•
United States	[b]	[b]	[c]	[c]

Wildlife tests						
Field tests—birds and mammals	Acute fish: LC50	Acute freshwater invertebrates: LC50	Fish: early life stage	Fish: life cycle	Aquatic organism accumulation	Simulated or actual field tests
•	•		•	•		•
•	•		•	•	•	
	•	•				
•	•	•		•	•	•
•	•	•			•	
	•	•			•	
•	•	•		•	•	
	•	•		•	•	
	•	•	•	•	•	
	•	•			•	
	•	•	•	•	•	•
	•	•			•	
•	•	•			•	•
•	•	•	•	•	•	•
c	b	c	c	c	c	c

[a]Cells that contain a "bullet" signify that a test was listed in a country's published data requirements. While this code suggests general equivalence between foreign and U.S. standards, it does not imply that the foreign requirement is identical to the corresponding standard listed in the Code of Federal Regulations. In most instances, the registration guidelines we reviewed did not provide sufficient specificity for us to make that determination. Empty cells indicate that a specific test was not cited in a country's registration documentation and thus imply that the test is not required for registration.

[b]Test is required.

[c]Test is conditionally required.

Table 2.6: Beneficial Insect Studies[a]

	Insect studies		
Country	Honey bee acute contact: LD50	Honey bee—toxicity of residues	Field testing for pollinators
Australia			
Austria			
Belgium			
Canada			
Denmark			
Finland	•		
France			
Germany	•		•
Greece	•		
Italy	•		
Japan			
Netherlands			
Norway	•		
Portugal	•		
Spain	•	•	
Sweden	•		
United Kingdom	•	•	•
EEC	•	•	•
United States	b	b	b

[a]Cells that contain a "bullet" signify that a test was listed in a country's published data requirements. While this code suggests general equivalence between foreign and U.S. standards, it does not imply that the foreign requirement is identical to the corresponding standard listed in the Code of Federal Regulations. In most instances, the registration guidelines we reviewed did not provide sufficient specificity for us to make that determination. Empty cells indicate that a specific test was not cited in a country's registration documentation and thus imply that the test is not required for registration.

[b]Test is conditionally required.

The two U.S. wildlife test requirements that were cited most frequently in the guidelines of OECD countries were "avian oral LD50" and "freshwater fish LC50" tests. Both tests evaluate acute toxicological effects—the former determining the dosage of the active ingredient at which 50 percent of the subject population of birds that ingest it (in a single dose) die, the latter determining the concentration in water at which 50 percent of the subject fish population die. In contrast to field tests that are often more costly and time-consuming, acute wildlife tests lend themselves more easily to standardized test protocols and well-defined outcome criteria; this

attribute may help account for the widespread acceptance of these tests among OECD countries.[8]

With regard to beneficial insect studies, all OECD countries required tests that examined a pesticide's effect on honeybees; only Germany, Spain, and the U.K., however, specifically listed at least two of the three honeybee studies listed under U.S. standards—that is, acute contact LD50, toxicity of residues, and field testing for pollinators.

Other Test Requirements

Data describing the chemical composition and physical properties of the active ingredient were required by all of the OECD countries whose guidelines we reviewed, as were residue chemistry tests. Efficacy tests—used to determine how well a pesticide performs its intended function—were required by all OECD countries except the United States.[9] Two types of studies required by EPA, reentry protection and spray drift, were rarely listed in the guidelines of OECD countries we examined, with only Australia requiring reentry protection data as part of its test requirements and only Germany requiring a spray drift study.

OECD Survey on Test Guidelines

Since we completed the matrix of data requirements presented in this chapter, OECD also undertook a similar effort. The OECD project consisted of sending a detailed survey to member countries on data requirements for plant protection products. The survey asked officials which data are requested for active ingredients, as well as formulations and products with food and nonfood uses; it also differentiated between requirements for products with indoor and outdoor uses. Seventeen countries and the Commission of the European Communities responded to the survey. Although too extensive to summarize here, the OECD project found the greatest similarities in the areas of chemical identity, physical/chemical properties, function/mode of action, and analytical methods. Toxicology and metabolism study requirements were also reported to be consistent across nations. The area with the most differences was ecotoxicology, where there was the lowest occurrence of data elements "always required" or "frequently required." The OECD findings complement those presented in

[8]As noted earlier, in October 1992 EPA revised its ecological effects requirements. Field studies are no longer required and will be more important as a monitoring tool. Such studies will only be required in "unusual" circumstances.

[9]Although EPA reserves the right to request such data, it does not require that manufacturers submit efficacy studies as part of the registration dossier. This may be one of the larger differences between the approach of EPA and other OECD nations. See the discussion in chapter 4 on efficacy studies where we discuss this issue in greater detail.

this chapter, providing additional detail on nonfood-use products and other uses, important aspects of any regulatory system.

European Economic Community Test Requirements

EEC member nations are now in the process of modifying their current data requirements to bring them into accord with recently adopted EEC standards. In each of the preceding tables, we compared the EEC test requirements with those of the United States. A perusal of tables 2.1 through 2.6 quickly confirms that if EEC member countries are successful in bringing their national standards into compliance with EEC guidelines, they will also be moving towards greater harmony with U.S. pesticide registration standards. (Proposed EEC test standards matched U.S. tests listed in tables 2.1 through 2.6.)

OECD Country Perspectives on Data Requirements

As part of our country visits, we asked foreign regulatory officials to discuss salient features and issues relating to their country's data requirements and test protocols. The remainder of this section of our report highlights points raised in these interviews.

Swedish officials told us that KemI, the agency in charge of Sweden's pesticide registration, maintains the position that its data requirements should serve as a guide for applicants by suggesting the types of test data that would provide evidence of their product's necessity and safety. Consistent with this philosophy, KemI accepts studies done according to OECD, EPA, and German protocols. KemI does not refuse to consider tests that follow protocols other than these three, although one administrator told us that they might find the results of such tests difficult to evaluate. Typically, the health and toxicity studies conducted in another country are acceptable; however, certain types of ecotoxicity tests might require modification. For example, soil degradation tests performed to meet U.S. requirements would most likely not be acceptable in Sweden due to differences in soil temperatures in the two countries. Sweden might also require an additional soil degradation test performed at a lower temperature.

German regulatory officials told us that the data requirements for registering a pesticide in their country are stricter now than they were in the past, and that, in consequence, data generated at an earlier time probably would not meet current standards. With regard to international comparability of data requirements, German officials told us that they believe there are few differences among nations. They pointed out that

chemical companies producing for the international market register their products in many places and, to the extent possible, produce the same data package for all countries. They noted that German requirements may specify one test but that, in a registration dossier, they may receive two sets of results from the registrant because EPA requires those tests.

While Greek authorities believe toxicology tests are broadly similar, they told us they prefer that efficacy trials be done in Greece—although studies done in countries with a similar climate (for example, other southern Mediterranean nations) are acceptable in cases where the product has been approved by at least two of these nations. They consider efficacy data to be particularly important because the average farm size in Greece is 5 hectares, spread over 10 different plots. These plots are farmed using intensive agricultural practices and crop rotation. The government of Greece is concerned about rotation practices because pesticide residues can remain in the soil for several growing seasons.

Italian officials believe that Italy's data requirements do not usually differ from those of other EEC nations. They told us that there is unofficial agreement among nations concerning the types of tests required for registration. Italy places great emphasis on efficacy testing; if registrants do not provide efficacy tests satisfactory in scope, the Italian Institute for Plant Pathology will perform such tests. Italy accepts both EPA and OECD protocols; if a protocol has not been established for a particular test, representatives of the Ministry of Health meet with registrants and develop an agreed-on protocol.

Spanish officials told us they accept studies done according to different protocols, following what is often referred to as the mutual acceptance of data. One official noted that there is no set number of tests that are required before registration is granted. Rather, data submitted by registrants are reviewed and analyzed, and additional data may be requested if warranted. Registration officials also expressed concern about environmental and efficacy tests. They noted that there is less agreement among nations about the former, and cited problems applying environmental test criteria across different nations' soils and climates. They suggested that "orienting methods" may be more useful than strict guidelines.

Industry Perspectives on OECD Nations' Data Requirements

In order to gain a more complete perspective on OECD nations' registration requirements, GAO arranged two roundtable meetings with representatives of six chemical companies to discuss general registration issues. Because these companies market pesticides internationally, their representatives were able to offer some first-hand observations on the registration requirements of OECD countries.

The consensus among industry representatives was that, to a large extent, the harmonization of data requirements has already taken place. They said that their companies typically do a single set of studies that can then be submitted to different countries. Industry representatives stated that tests are too expensive to repeat for each country and that the same tests are, in fact, accepted by different nations. They estimated that approximately 80 percent of the data submitted by the different countries are the same, and that the 20 percent of intercountry data variation is attributable to environmental testing and, to a lesser extent, idiomatic approaches to the data.

Industry representatives told us that, unlike toxicology tests, environmental tests must be tailored to correspond to the unique climatic and geologic conditions of the registering country. Canada experiences colder temperatures than the United States, which means that its soil degradation studies must be performed at lower temperatures (3 to 5 degrees Fahrenheit versus 20 degrees Fahrenheit in the United States). Similarly, because Germany and the Netherlands are extremely attentive to the issue of groundwater contamination, they require more stringent leaching tests.

Several test regimens were cited by industry officials as being moderately atypical, including Japan's requirement for information on animal metabolites, Germany's emphasis on efficacy data and lysimeter tests, the Scandinavian countries' accent on environmental testing, and the United States' approach to carcinogens (that is, quantitative risk assessment). Further, these officials also noted that, as a practical matter, product efficacy data are not transferable and must always be collected on location in the registering country.

Industry representatives also told us that the format of the data dossier submitted to register a pesticide varies across countries. According to these representatives, EPA, for example, prefers to examine the details of experimental tests, and thus requires access to the raw data. Conversely,

some countries do not request the raw data, preferring that registrants submit only a study report or summary assessment of the data.

When asked how they select the countries where they register a product, company representatives stated that market factors drive such decisions. That is, the ability of a product to fill a particular market niche and the degree of competition from similar products were cited as the primary considerations when a manufacturer is seeking a country in which to register a product. One representative asserted that, given the expenses associated with developing and testing a product (several million dollars), it does not make economic sense solely to target weaker registration systems. To maximize profit potential, manufacturers told us that they attempt to sell their products in as large a market as possible, and that developing products that do not meet the standards of several nations would minimize this possibility.

Summary

Using registration guidelines supplied by OECD countries, we compared the types of data required to register a food-use pesticide in the United States with the data requirements of other countries. Broad concordance was found with respect to the types of data required to assess the chemical composition, physical properties, and toxicology of a test substance; however, there was somewhat less agreement on ecological and several "other" test requirements. Information obtained in discussions with regulatory officials in OECD countries and industry representatives substantiated the view that, with the exception of ecological and efficacy testing, the majority of data requirements are shared among OECD nations.

With regard to test protocols, the foreign officials we spoke with said that their countries accept data generated according to internationally recognized standards, such as those of OECD or EPA. Many of these officials also stressed the importance of efficacy data in their registration process, a position differing from that of EPA (which does not routinely evaluate such data).

This aspect of our investigation of international pesticide standards suggests that, while the areas of disagreement are relatively small, uniformity of all data requirements may not be achievable. Specifically, variation in geologic and climatic conditions probably precludes the adoption of a single battery of test requirements that would satisfy the needs of all countries.

Pesticide Regulatory Agency Structure and Personnel in OECD Nations

Introduction

This chapter addresses our second evaluation question, "What organizational structures do OECD nations have in place to evaluate pesticides, and how do these structures compare with that of the United States?" In the second chapter, we indicated that extensive agreement exists between the United States and many other OECD countries with respect to the types of test data used to conduct a toxicological evaluation of a pesticide. While data requirements are the cornerstone of a pesticide regulatory system, such requirements by themselves do not guarantee that a pesticide will be thoroughly reviewed prior to registration. Unless the agency charged with the task of registering pesticides has the organizational capacity and scientific personnel available to rigorously evaluate these data, its registration decisions must be viewed with some caution.

In this chapter, we discuss data collected in the course of country visits, as well as provide information on the U.S. pesticide regulatory system. Among the countries visited, we found important variations in agency structure and in the number of scientific personnel employed for the purpose of evaluating test data.

U.S. Pesticide Regulatory Structure

Pesticide regulation in the United States has undergone several cumulative transformations since the Congress enacted the Insecticide Act of 1910. This act had, by today's standards, a relatively limited agenda, which was mainly to prevent the mislabeling or adulteration of insecticides and fungicides. In 1947, it was replaced by the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA).

The objective of the original FIFRA legislation centered on assuring product performance and protecting users from acutely dangerous pesticides. By 1962, pesticide registration requirements consisted of securing USDA approval of the label to be used on pesticide containers and obtaining an FDA residue tolerance indicating how much of a pesticide could remain on or in a raw agricultural product.

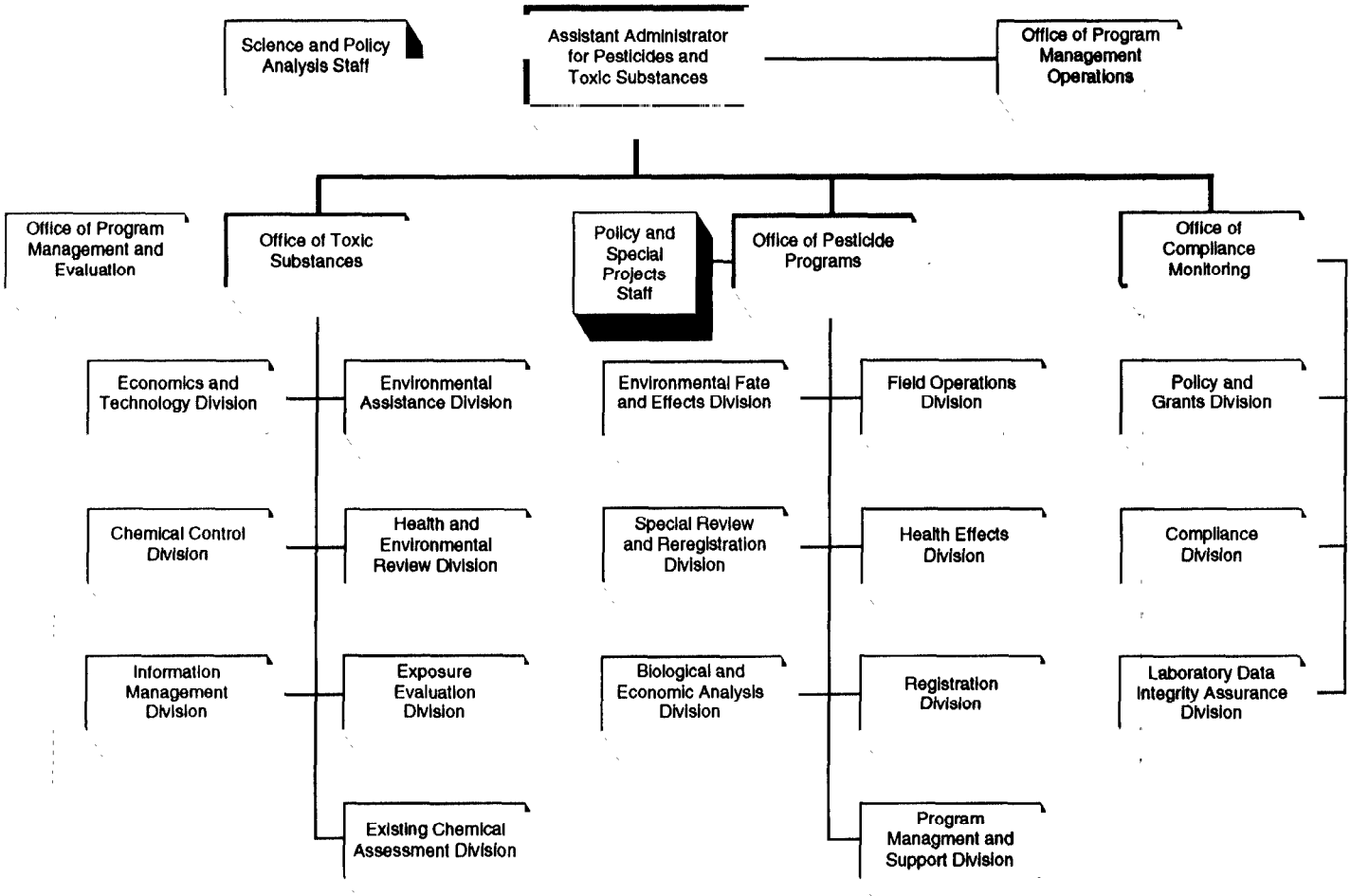
Jurisdiction over pesticide regulation was passed to the Environmental Protection Agency (EPA) in 1970, which signaled a concurrent shift in regulatory focus. Under extensive 1972 FIFRA amendments, in addition to demonstrating that a pesticide effectively controlled weeds or insects, manufacturers were now required to provide data that showed that residues would have no "unreasonable adverse effects" on human health or the environment.

Aided by more precise instruments and sophisticated methods, the field of health effects testing has evolved in the United States and abroad, progressing from primarily assessing acute effects (those occurring immediately after exposure to a pesticide) to gauging effects, such as cancer, that may result from intermediate and long-term exposure. The scope of health effects testing has continued to expand, as evidenced by the recent regulatory attention given to a pesticide's potential allergenic effects.

As EPA's pesticide regulatory system has evolved, a third substantive area has received increasingly greater attention—that is, the impact of pesticide use on the environment. Environmental tests include studies that measure a pesticide's effect on the soil, nontarget insects, birds, fish, and mammals. Although this field of testing has developed rapidly in comparison with that of health effects testing, certain tests are inherently less amendable to standardization because of the difficulty of generalizing between different ecosystems.

EPA's wide range of concerns are reflected in the current organizational structure of the Office of Pesticides Programs (OPP), which oversees pesticide registration. (See figure 3.1.) OPP employs approximately 800 persons, 300 of whom are involved in the evaluation of test data.

Figure 3.1: EPA's Office of Pesticides and Toxic Substances



Source: EPA

Swedish Pesticide Regulatory Structure

Sweden's pesticide control system began in 1934 and, like the early registration program in the United States, focused on the efficacy of pesticides. In 1964, a registration system was established, and registrants were asked to provide health and environmental data on compounds. Swedish authorities began to exercise more control over pesticides in 1985 when the Swedish Chemicals Inspectorate (KemI) was created with a

mandate to impose stricter standards on chemicals, including pesticides. KemI is essentially a financially self-sufficient institution; it receives only a token annual government subsidy of 1,000 Swedish crowns (about U.S. $175). The remaining operating expenses are met by levying registration fees on industry. As explained by one KemI administrator, the 1985 law placed increased emphasis on preventing injuries that could arise from chemical exposure. Other changes brought about by this legislation included limiting approvals for compounds to a 5-year period, requiring that all products on the market at that time be reregistered by the end of 1990, reducing pesticide use by 50 percent by 1990, and requiring farmers to attend an approved 3-day training course before being allowed to purchase pesticides and farm equipment used for pesticide applications.

Compared with EPA, KemI is a relatively lean organization, employing a staff of 104 persons. Its organizational structure includes offices for product registration, inspection, approval, research, and chemical control. KemI employs 17 full-time scientists to do pesticide evaluations. In addition, KemI has engaged university scientists to complete health hazard or environmental hazard reports. Because there are relatively few personnel, the registration process has been structured to maximize its effectiveness. KemI officials told us that to require and examine data from the entire battery of test requirements, only to find at the end of the evaluation that the product poses potential hazards, is a waste of both the Inspectorate's and the registrant's resources. It is costly for a manufacturer to conduct numerous tests for a product that ultimately cannot be marketed. Similarly, from the Inspectorate's standpoint, it is inefficient to have scientists spend time evaluating a complete data package when adverse effects uncovered by certain tests would preclude approval of a compound. KemI believes that the best way to conduct an evaluation is to identify compounds with unacceptable attributes early in the registration process. Hence, to be granted registration status, compounds must pass a tiered series of evaluations—failure at any point in the sequence terminates the process.

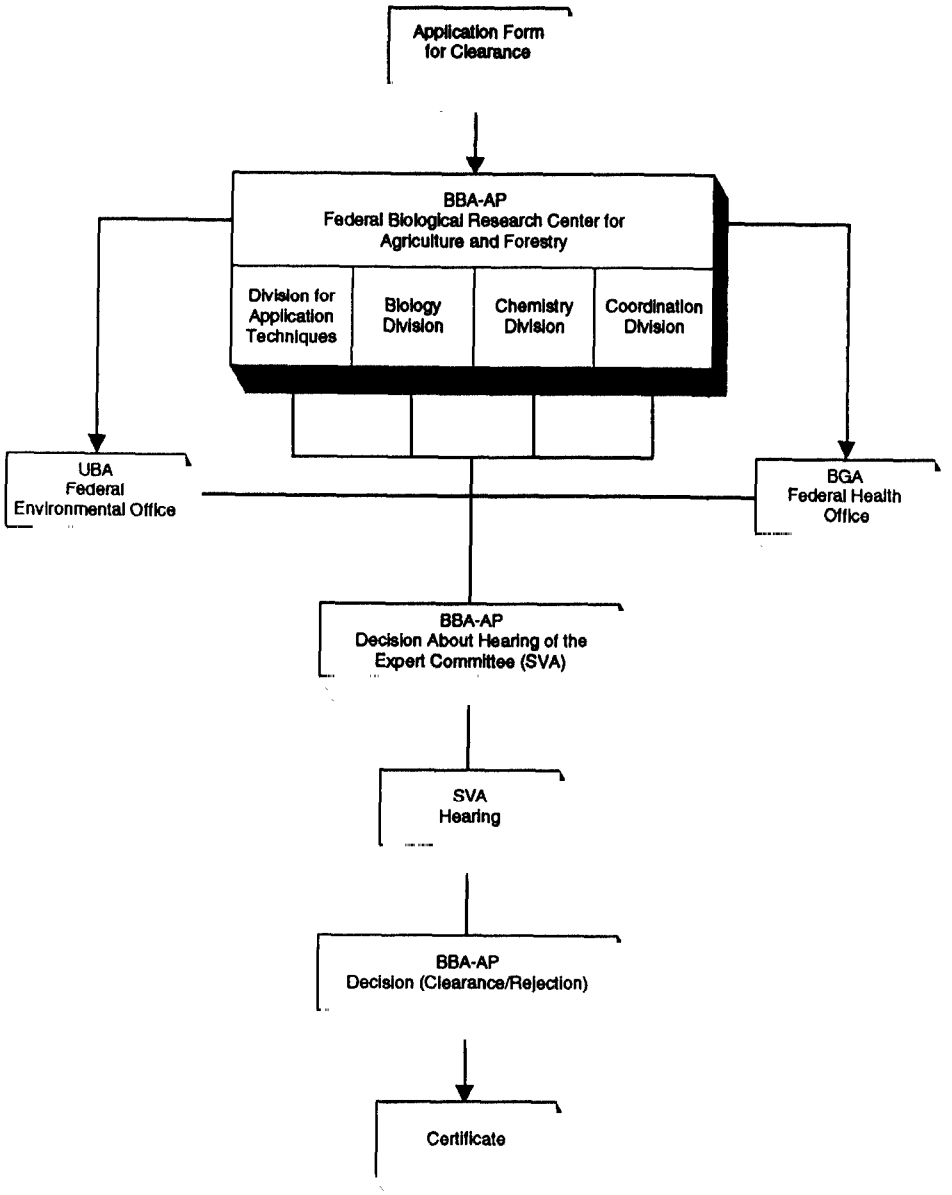
Sweden also augments its evaluation capabilities by collaborating with other Scandinavian countries. Although registration in another Scandinavian country does not automatically lead to registration in Sweden, KemI officials stated that by working closely with neighboring countries they are able to share some of the burden of evaluating different pesticides.

German Pesticide Regulatory Structure

Germany first enacted legislation requiring pesticide registration in 1937. During the succeeding 51 years, pesticide registration in Germany was done on a voluntary basis. German regulations were updated in 1968, when the Plant Protection Act was passed, and again in 1986. The latest revisions to German law created the Federal Environmental Office (UBA), which was given responsibility for reviewing new tests required to measure a pesticide's effect on soil, groundwater, or other environmental elements. The act placed a legal obligation on users to acquire application skills.

Of the five countries we visited, Germany appeared to have the most extensive institutional structure in place to evaluate pesticides. Three separate agencies are involved in the German registration process: the Federal Biological Research Center for Agriculture and Forestry (BBA) through its Department for Plant Protection and Application Techniques (BBA-AP), the Federal Environmental Office (UBA), and the Federal Health Office (BGA). The registration process is initiated when a registrant submits an application to BBA. BBA then sends copies to UBA and BGA for evaluation (with each agency focusing on different aspects of the data package). After each agency has reached a decision, they collectively decide whether to grant final approval; each agency must agree with this decision. Figure 3.2 demonstrates how these three agencies conduct the registration process.

Figure 3.2: Structure of the German Pesticide Registration System



Source: Germany's Biological Research Center for Agriculture and Forestry

BBA

Within BBA, BBA-AP is the lead division in the German pesticide registration system and is responsible for granting final approval of a product. BBA-AP employs a staff of approximately 130 persons, including about 40 scientists. It is comprised of four divisions: Application Techniques, Biology, Chemistry, and Coordination. The Division for Application Techniques is responsible for testing application machinery and equipment; it also handles questions concerning the use of pesticides. The Biology Division has several tasks, one of which is to evaluate all efficacy data. In addition, the Biology Division investigates the effects of a pesticide on beneficial organisms, soil fauna, and wild mammals. The Chemistry Division examines the chemical composition and physical properties of pesticides and evaluates data on the residue behavior of compounds. The Chemistry Division also assesses environmental fate data—that is, studies that show how a pesticide degrades in soil, water, and air. Finally, the recently established Coordination Division coordinates various internal, national, and international tasks pertaining to pesticide registration.

BGA

The Federal Health Office, or BGA, consists of six separate institutes. BGA's primary mission is to protect the health of humans and animals; thus, its role in the review process is to evaluate toxicology and residue data, as well as examine issues relevant to pesticide application. German officials told us that it is common practice for BGA to request additional toxicology data. (Virtually all applicants have to submit additional data.) Although the overall process takes between 1 and 1.5 years to complete, once all the data requirements are met, BGA typically renders a decision on a product within 5 months.

In 1991, applications for approximately 200 compounds were submitted for registration in Germany. BGA refused consent to about 15 percent of these applications. The reasons for refusal were generally formal (involving, for example, issues relating to "good laboratory practice" and insufficient data). Each year applications for about five or six new active ingredients are also submitted.

UBA

A third agency involved in the registration of pesticides is the Federal Environmental Office, or UBA. Established in 1987, UBA is charged with implementing German law that covers environmental concerns, including the quality of groundwater. After receiving a copy of the application from BBA-AP, UBA evaluates the data for possible adverse environmental effects

caused by the pesticide compound. Since 1987, UBA has reviewed at least 900 pesticide products and has refused consent to 8 active ingredients involving at least 20 products.

Officials from UBA expressed the belief that the environment, and especially groundwater, receives greater attention in Germany than in the United States. It was their opinion that EPA is more attuned to human health measures. With respect to test protocol for environmental tests, UBA officials said that EPA guidelines are acceptable. As far as environmental test protocols are concerned, they felt there are basically no differences between EPA, OECD, and the EEC.

Spanish Pesticide Regulatory Structure

Spanish officials told us that their registration system was created in 1944 for the purpose of ensuring product efficacy. In 1973, Spain first required registrants to provide environmental test data; in 1976, World Health Organization (WHO) standards for pesticide classification were adopted, thus providing a mechanism of control over where highly toxic pesticides are used. The Spanish system was expanded in 1983 and 1984, when public health and safety data were first required from registrants. Government officials told us that staff were hired in 1983 to permit a more intensive review of pesticide registration applications. Pesticide registration in Spain is coordinated by the Ministry of Agriculture and Fisheries, Registry of Phytosanitary Products Office, which oversees work performed by six committees. Support for toxicology and residue data reviews is provided by staff employed by the Ministry of Sanitation and Consumption. The government also uses reports published by international organizations as a point of reference when conducting toxicological evaluations.

Spanish officials reported that they review materials on both the active ingredient and the formulation, requesting that registrants provide both a summary of these materials and supporting documentation. The Ministry of Sanitation and Consumption's Chemical Safety Unit, with a staff of 10, is responsible for reviewing toxicity data submitted in support of a pesticide registration. These staff also receive assistance from an outside review panel that is comprised of toxicologists and an industry representative. After this review, the compounds are classified according to toxicity level, a label is approved, and a maximum residue limit (MRL) is determined by a joint residue committee comprised of staff from the Ministry of Agriculture and the Ministry of Sanitation and Consumption.

Analytical chemistry, ecotoxicology tests, and efficacy data are reviewed by a separate committee, under the auspices of the Ministry of Agriculture. Spain mandates that field trials be conducted domestically, although in certain instances trials conducted in other nations may be reviewed to determine if the product is suited to Spanish crops. An industry representative indicated that chemical companies, in collaboration with regional government centers, do nearly all the field testing of products. The primary concerns that drive the Ministry's review of ecotoxicology data are how a product is to be used, application rates and doses, specific conditions under which a product can be used, and potential environmental impact.

Once a pesticide has passed through this review process, it is approved for a 2-year provisional period, during which time staff in regional government agricultural centers keep track of use patterns and any problems farmers encounter. If no problems emerge during this period, a compound is granted a permanent registration, which is valid for 5 years. After 5 years, the compound is subject to a reregistration process that is overseen by the Ministry of Agriculture.

Spanish officials noted that they are in the process of improving their pesticide evaluation capabilities. One factor encouraging this change is that Spain will be asked to review 10 pesticides under the pending EEC reregistration initiative. The Ministry of Sanitation and Consumption plans to add 3 people to its current staff of 10 to help facilitate the review process. Ministry officials expect that several observers from other EEC nations will serve as reviewers of their work.

Greek Pesticide Regulatory Structure

Prior to 1977, pesticides were not subject to government regulation in Greece. The 1977 legislation outlined cursory registration guidelines and the responsibilities of different government ministries in overseeing plant protection products. In 1988, Greece's pesticide law was updated. One of the key modifications made in the law was that the types of toxicological data a registrant had to submit in order to register a pesticide were specified for the first time. The 1988 legislation does not, however, specify wildlife test results that registrants are to submit as part of a registration application. In addition, Greek officials told us that pesticides that had been on the market more than 5 years before the 1988 legislation went into effect are not subject to the new registration standards.

The Ministry of Agriculture's Plant Protection Department is the lead organization in Greece for pesticide registration. It works closely with the Benaki Institute's Department of Pesticide Control and Phytopharmacy, as well as with the High Commission on Pesticides. The Benaki Institute has operated since 1931, and its work is mainly financed by the government through the Ministry of Agriculture. The High Commission on Pesticides was founded by the Ministry of Agriculture and is, by law, comprised of representatives of relevant departments at Athens University, state-operated laboratories and offices, and the Ministry of Agriculture.

Greek officials stated that the toxicology data they review are similar to data requested by other EEC nations. They also stated that they request that registrants adhere to the OECD Guidelines for Testing of Chemicals. The Plant Protection Department of the Ministry of Agriculture, with seven full-time professional employees, reviews all registration applications, oversees the monitoring and enforcement process, and maintains contact with international organizations. Principal responsibility for reviewing toxicity data lies with the Benaki Institute's Department of Pesticide Control and Phytopharmacy, whose 15 scientists review pesticide applications and are involved in some related research. The Department has five laboratories: efficacy evaluation (four staff), residue analysis (six staff), physical and chemical properties (three staff), and toxicology and fungicides (one staff member each). Department spokespersons reported that they anticipated adding staff to meet the demands of annually reviewing six pesticide-active ingredients under the EEC reregistration initiative.

The Plant Protection Department and the Benaki Institute issue reports based on their reviews, which are sent (along with summaries of the application and test results) to the High Commission on Pesticides, an advisory group. Current High Commission members include two professors from the Agricultural University in Athens, a professor from the School of Medicine, a dietary chemist from the Polytechnic Institute, the Manager of Hygiene of the Department of Health, and the General Manager of the Ministry of Agriculture's Plant Protection Department. The Ministry of the Environment is not represented in the pesticide review process.

The High Commission on Pesticides also issues a report that is sent along with other prepared reports to the Minister of Agriculture, who then makes the final decision on whether to register a pesticide. The decision is published, as is the approved wording for the product label. None of the reports or evaluations issued to the minister during the review process are

published, although the government has the legal right to release results of analyses and other verifications if it so chooses. The government does not publish an updated list of pesticides approved for use in Greece (although such a list is published privately); however, Ministry of Agriculture officials told us that they were currently in the process of computerizing registration information and hope to have a list "on-line" by 1993.

Italian Pesticide Regulatory Structure

Italy enacted legislation in 1968 that created a formal pesticide registration system. Legislation passed in 1990 in response to EEC directives significantly modified several aspects of the registration process, resulting in tighter control over older products. Pesticide registration is overseen by the Public Health Ministry working through a coordinated committee that reviews pesticide applications for human health dangers and agricultural threats.

In Italy, the Ministry of Health is responsible for registering pesticides and monitoring their use. The ministry is advised by a committee composed of representatives of its own agency, the Ministry of Environment, Ministry of Agriculture and Forestry, Ministry of Industry and Labor, and the Scientific Institute for Plant Pathology. The committee evaluates the submitted data for efficacy, effects on human health, and effects on the environment. The committee can request assistance from nongovernmental sources such as universities, but most often it reviews and evaluates the data itself.

After completing its evaluation, the committee recommends an action to the Ministry of Health, which in turn makes and publishes the final decision. Officials told us that it takes from 2 to 5 years (the average is 3 years) to evaluate a new active ingredient, and about 1 year to evaluate a new formulation comprised of known active ingredients.

In 1991, the Ministry of Health further specified the tests required to register a pesticide, and consequently most applications are now complete when submitted. In 1991, for example, only 20 percent of the applications had to be returned to manufacturers for additional data. In prior years, the proportion of incomplete applications was much higher. An official stated that, even when submitting completed applications, manufacturers can sometimes hide a pesticide's harmful effects. Existing scientific literature frequently reveals these effects.

Prompted by EEC directives, Italy has since 1990 required that older pesticides be reregistered and reevaluated. Prior to 1990, reevaluation was required only occasionally, usually when a problem was identified. The original deadline for completion of the newly required reregistration was 1992; however, officials acknowledged that the process was not likely to be completed until at least 1995.

Italy's principal policy direction on data requirements is to conform to EEC requirements. The government expected its laws and directives to be in compliance with EEC standards by July 1992. Although an official expressed Italy's interest in reducing pesticide use, a national plan for a reduced and integrated use of pesticides, enacted into law in 1987, was inadequately funded and allowed to expire.

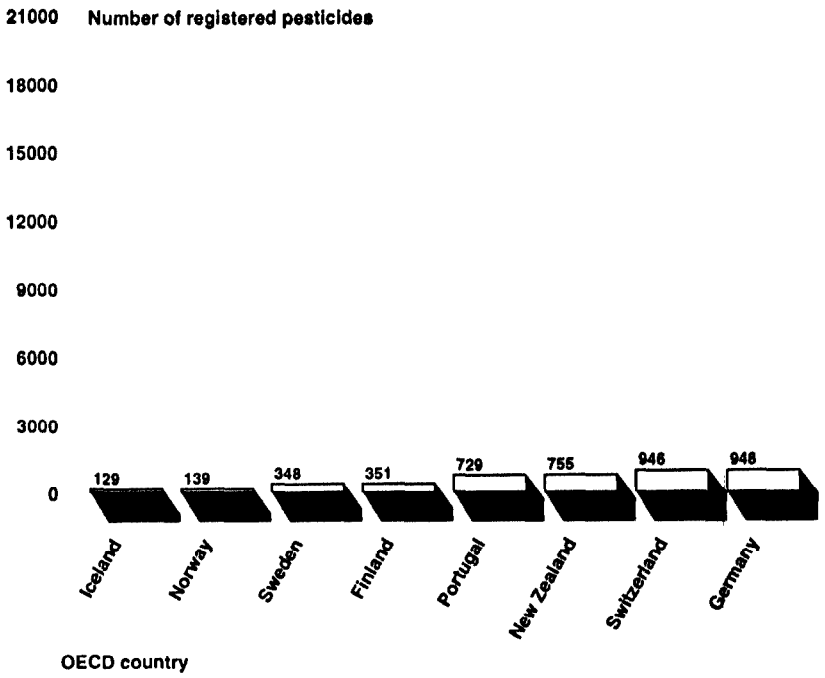
Staff Size and Number of Registered Pesticides in OECD Countries

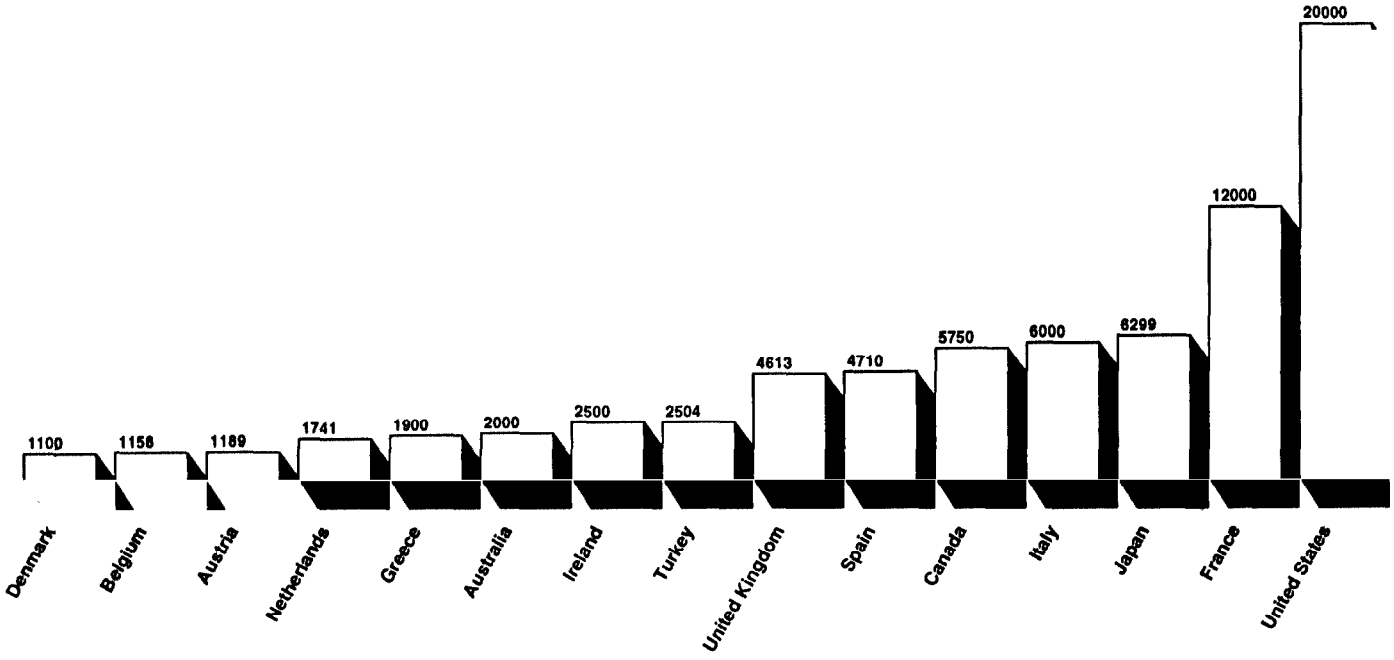
OECD member nations differ widely in geography, climate, soil type, and quantity of arable land. The size and importance of the agricultural sector also vary among nations. Such factors can affect the quantity and the number of different types of pesticides needed to sustain agriculture. For example, a country that has a cold and humid climate may have less need for insecticides and fungicides, but a greater need for herbicides to control weeds.

We asked State Department staff stationed in OECD countries to obtain a numerical estimate of the number of pesticide products registered in their host countries. The results of this survey are displayed in figure 3.3. Product registrations in 1991 ranged from 129 in Iceland to 20,000 in the United States. Figure 3.3 is interesting not only because it shows a wide range in the number of registrations granted by the various OECD countries, but also because it provides a rough indication of the workload that has confronted pesticide regulatory officials in these countries. That is, if it can be assumed that the acceptance/rejection rates of registration applications are generally comparable among OECD countries, then the number of registrations a country has granted provides some indication of the number of pesticide evaluations it has conducted.[1]

[1]We did not collect data that would allow us to estimate the "rejection rate" of pesticide registration applications in various OECD countries. Such data, if it were available, might be an indicator of the relative stringency of the respective registration systems. There are numerous problems with collecting information of this type, however. In some countries, the rejection of a product is treated as a confidential matter between registrant and governmental regulatory agency. Further, rejection rates do not sufficiently account for registration applications that are never completed. Such "pending" registrations may languish in the system for many years.

Figure 3.3: Number of Registered Pesticide Products in OECD Countries[a]





[a]Registration figures for Luxembourg were unavailable. The numbers presented here represent pesticide products with the exception of that for Norway, which reported only registered active ingredients.

It would seem likely that countries that have greater need for pesticides might grant a larger number of registrations, and thus also have larger staffs and more elaborate organizational structures to evaluate pesticides. This expectation is clearly not supported by the information we were able to collect during our country visits. In terms of the number of pesticide products registered, four of these countries can be rank-ordered as follows: (1) Spain [4,710], (2) Greece [1,900], (3) Germany [948], (4) Sweden [348].[2] Yet, in terms of number of government staff assigned to evaluate pesticides, these same countries fall into the following order: (1) Germany, (2) Sweden, (3) Spain, (4) Greece. Germany's BBA-AP, one of three German agencies responsible for evaluating test data, employs a staff of 130 scientists. KemI, which reviews Sweden's pesticide registration materials, employs a staff of approximately 100, 17 of whom evaluate test data. In contrast, Spain's Chemical Safety Unit, an agency with similar

[2]The numbers of active ingredients registered by the countries are as follows: Spain (480), Greece (320), Germany (216), and Sweden (126).

responsibilities, employs a staff of 10 scientists. Finally, the Benaki Institute, which reviews pesticide data submissions for the Greek government, has a staff of 15 that includes one full-time and two consulting toxicologists, who serve together as members of an advisory panel.

Summary

The 1980's saw the movement to harmonize the pesticide registration process gain momentum. This policy initiative provided the impetus for many European countries to significantly reexamine their pesticide regulatory systems. For some countries, this has meant establishing greater evaluation capabilities, while for others it has meant considerable restructuring of existing institutions.

All the countries we visited have had a pesticide registration system in place for more than a decade; however, until recently, the registration systems in several of these countries could have been characterized as akin to licensing bureaus, rather than being full-fledged toxicological evaluation programs. At present, these countries all conduct some form of toxicological evaluation prior to registering a product. EEC harmonization directives in the mid-1980's also caused them to upgrade their systems. This process is not yet complete, and in accordance with EEC harmonization initiatives, several countries we visited anticipated making further improvements in their regulatory systems during the coming decade.

We found differences in the ways the regulatory systems described in this chapter structured the evaluation process. Some countries, notably Sweden and Germany, relied primarily on government scientists to assess test data. Spain and Greece, on the other hand, relied to a greater degree on the advice of outside experts. These organizational differences seemed to be driven by two factors: financial resource constraints and the maturity of the regulatory system.

Staff size was inversely related to the number of pesticides that were registered in the countries we visited. Regulatory systems with small scientific staffs registered as many, or more, pesticides as systems with larger staffs. This fact, when considered in conjunction with the previously mentioned staffing disparities, suggests that toxicological-evaluation capabilities may not be uniform among OECD countries. While it may indeed be possible to compensate for agency staffing shortages by utilizing outside experts—or, in the case of Sweden, by structuring the evaluation

process in such a way as to limit the number of pesticides that are given detailed review—staff size is still a factor that must be considered in any attempt to harmonize pesticide registration decisions and product reviews.

Evaluation Issues: Risk Assessment and Risk Management

This chapter addresses our third evaluation question, "What risk assessment and risk management procedures are used in OECD nations, and how do they compare with those of the United States?" Our investigation found differences in approach to, and philosophy used in, assessing and managing the risks associated with pesticides. With regard to risk assessment, we found that many OECD countries lack transparency in their evaluation procedures, a fact that precluded our making a systematic inter-country comparison on this dimension. Carcinogenic risk assessment, however, was identified by both U.S. and foreign regulatory officials as an area where significant scientific differences in approach exist. In the sphere of risk management, we found that pesticide regulatory systems reflect national priorities, such as concern over potential groundwater contamination, the overall quantity of pesticide use, and cost-benefit considerations. Such factors may influence the range of pesticides that gain registration in the United States and other OECD countries.

Risk Assessment

In the foregoing chapters, we have described the process of pesticide evaluation in very general terms—that is, scientists review animal and environmental studies submitted by registrants and use this information to assess the potential risks of a pesticide to human health and/or the environment. In practice, in assessing and quantifying the risk associated with a given pesticide, scientists observe a formalized protocol that involves analytically reviewing test data on four dimensions: (1) hazard identification, (2) dose response, (3) exposure, and (4) risk characterization. The first three of these components address the following concerns: Is exposure to the pesticide associated with a pattern of adverse effects in humans (for example, cancer or birth defects)? At what level(s) of exposure does it produce these effects? What avenues of exposure pose potential risks (for example, through inhalation or skin contact), and how much of this compound is a person likely to be exposed to? Risk characterization requires integrating results from the first three components. The end result of the evaluation process is to determine the nature of the risk posed by exposure to a compound; the conditions under which it may be safely used; and, ultimately, the advisability of granting registration.

Transparency of Regulatory Decisions

In discussions with U.S. and foreign regulatory officials, we were told that the risk assessment process in the United States, as compared to those in other OECD countries, has been procedurally more open or transparent.

Such transparency has manifested itself in two ways. First, many of the rules that direct experts in their evaluation of test data have been codified in written form. EPA has, for example, published extensive guidelines that spell out rules for interpreting data that relate to the carcinogenic, mutagenic, and other toxicological properties of chemical compounds. The intent of such guidelines is to bring greater consistency to the evaluation process and thereby ensure that various experts assessing the same compound will reach similar conclusions, as well as that different compounds will be judged by the same standards. The EEC is in the process of finalizing detailed guidelines for use in member states' reviews of pesticide active ingredients and formulations. Guidelines we reviewed emphasized a tiered process that should lead to more uniform standards and reviews across EEC member nations.

A second aspect of procedural transparency relates to the availability of post-evaluation explanations of regulatory decisions. The United States' risk assessment process allows both the registrant and the public access to the rationale that led to the acceptance or rejection of a product for registration. Pesticide registration decisions made by scientists and regulatory officials are published in the Federal Register and are available for public examination. As part of the EEC's efforts to harmonize pesticide reviews, its draft documents have called for publication of such decisions, including summaries of both the documentation evaluated and the scientific rationale used in reaching conclusions. The draft document notes that this type of requirement, if agreed to by member states, may require the amending of the relevant council directive (91/414/EEC). Such decisions could possibly be published in the "C" series of the Official Journal of the European Communities.

Evaluation Procedures in OECD Countries

German officials consider data interpretation and evaluation in their country to be a less formalized process than that practiced by EPA. In their view, EPA produces documents that describe in great detail the evaluation procedures used, whereas the German system relies more on a case-by-case analysis. In Germany, rather than relying on written documents that specify the steps used to evaluate data, a new scientist learns how to do an evaluation by undergoing an apprenticeship. In support of this approach, German officials cited the fact that scientific practice is continually being changed and modified, thus quickly rendering many written guidelines obsolete.

German officials told us that they try to work closely with the registrant during the initial stages of the evaluation process in order to develop an appropriate sequence of studies. An initial set of core tests is specified; then, on a case-by-case basis, additional tests may be requested. Final registration decisions are made after consulting an expert panel whose members have reviewed the test data. It is important to note, however, that the rationale behind the panel's final decision is considered a confidential matter between the German review board and the registrant—the reasons for the decision are thus not made public, although government authorizations are published in the Federal Law Gazette.

Officials from the Greek Ministry of Agriculture told us their agency publishes only the registration decision and the facts to be contained on the product label. Governmental reports produced as part of the evaluation process are not published or made publicly available. Officials from the Benaki Phytopathological Institute reported that their approach to carcinogenic data evaluation differs from that of EPA. The officials we interviewed stated that they look at epidemiological studies and probable exposure to a pesticide, as well as studies done on three different types of lab animals, to determine probable carcinogenicity.

Italy does not have explicit guidelines for evaluating test data. For example, they have not established thresholds or standards for determining whether the environmental effects of a pesticide are acceptable. A panel of experts is now in the process of developing standards for assessing environmental effects and expects to complete its work by the end of 1993. According to government officials, health concerns generally rank higher in the evaluation process than environmental concerns. No distinction is made between cancer and other health risks; all are evaluated by the same methods.

Sweden has enhanced the objectivity of its evaluation process by establishing cut-off criteria for many test requirements. For example, acute toxicity is now divided into four levels: very high, high, medium-to-moderately high, and moderate. Very high acute toxicity is defined as an $LD_{50} \leq 25$ mg/kg for the acute oral toxicity test, an $LD_{50} \leq 50$ mg/kg for the acute dermal toxicity test, and an $LC_{50} \leq 0.25$ mg/l for the acute inhalation toxicity test.[1] Test results that place a compound in the

[1]LD50 (lethal dose 50) and LC50 (lethal concentration 50) are widely used toxicological parameters, they refer, respectively, to the dosage and concentration in water that would cause a 50-percent mortality rate in the test population under specified conditions.

"very toxic" category are considered unacceptable by KemI and will result in the outright rejection of a registration application.

The issue of transparency also surfaced at a recent OECD-sponsored workshop on pesticide reregistration. Participants at this workshop suggested that harmonizing data review procedures holds promise as a means to speed up the process of reregistering pesticides by allowing countries to share the burden of evaluating data. It was agreed, however, that before such collaborations are possible, more information is needed that describes how different countries conduct their data reviews. It was recommended and agreed that a pilot project be initiated to compare existing national practices and "determine where major similarities and differences in scientific evaluation may occur, and where necessary, to develop appropriate solutions."[2]

The pilot project will select a small number of agricultural pesticides that have undergone a recent comprehensive data review by multiple countries, and whose data bases are not overly complicated by unresolved scientific and/or political issues. The project will compare existing data reviews in the following test areas: physical chemistry, toxicology, environmental fate, and ecotoxicology.

Summary

A theme that recurred in many of our discussions with regulatory officials from various OECD countries related to what they perceived as the greater flexibility of their evaluation process in comparison to the procedures followed by EPA. Officials from these countries stressed that they do not take a "cookbook" approach to data evaluation; rather, aside from certain core tests, their preferred method is to work in collaboration with the manufacturer when evaluating a compound. In this sense, the procedural transparency that EPA sees as a virtue of its evaluation system may be perceived as being overly rigid by some OECD countries, although it would not necessarily preclude examining such chemicals on a case-by-case basis.

The general absence of documentation outlining the rules that guide the evaluation of pesticide compounds, as well as the unavailability of post-decision rationales (for example, which aspects of the test data regulators found most problematic), prevented us from systematically comparing EPA evaluation procedures with those of other OECD countries.

[2]Letter from the OECD's Bill L. Long to OECD Permanent National Delegations on this pilot project, December 9, 1992.

However, most U.S. and foreign officials identified the area of carcinogenic risk assessment as an aspect of the evaluation process where significant differences in approach exist.

Assessing Carcinogenic Risk

It is often difficult to experimentally detect a relationship between exposure to a chemical compound and the contraction of a chronic disease. For example, the development of a chronic disease like cancer can require long periods of toxic exposure before symptoms are evident. Unlike acute and subchronic studies that assess immediate or short-term adverse effects, chronic studies are aimed at assessing the adverse effects resulting from prolonged and repeated exposure to a substance. Although the average chronic feeding study spans a period of 2 years, sufficient numbers of animals (usually rodents with short life spans) must survive long enough for the development of late-appearing diseases. Thus, experiments designed to measure a compound's potential in this regard may be relatively costly and time-consuming.[3] The typical chronic feeding study lasts 2 years and involves 800 animals (4 dose levels of a pesticide, given to 2 species, divided by sex, with 50 animals in each group). Despite this large sample size, if a chronic endpoint has a low incidence rate (for example, if only 5 percent more tumors are found in the experimental group than in the control group), the connection between exposure to a chemical substance and the contraction of a chronic disease may not be either evident or statistically significant.[4]

One method that enhances experimental sensitivity—that is, the ability of an experiment to detect small differences in disease formation between the experimental and control groups—is to increase the sample size. Using a large number of test animals when conducting experiments makes it easier to demonstrate a statistically significant relationship between exposure to a substance and a given biologic response. This approach has limitations, however. Significantly increasing sample size beyond what is now commonly used would drive up the already high cost of toxicology testing; this factor, when coupled with growing public concern over the

[3]During long-term studies, test animals may die for a variety of reasons not directly related to exposure to a pesticide. For example, an infectious disease can decimate the test population so that few animals reach old age.

[4]Some researchers estimate that where the true incidence of tumors is less than 7 percent, long-term feeding studies may not be able to reliably detect a pattern of carcinogenicity. See A. Blair et al., "Carcinogenic Effects of Pesticides," in S. Baker and C. Wilkinson (eds.), The Effects of Pesticides on Human Health (Princeton, N.J.: Princeton Scientific Publishing Company, 1990), p. 230.

use of animals in experiments, imposes practical limitations on the use of this strategy.[5]

Maximum Tolerated Dose

Another way of increasing the likelihood of observing a chronic effect such as cancer involves administering what is termed the maximum tolerated dose (MTD) of a pesticide in experimental trials. MTD is the highest dose animals are subjected to in testing (with lower doses also being administered as part of the experimental design). MTD is determined by continually ratcheting upward an animal's intake of the compound until severe effects are observed. The rationale behind this approach is that at higher doses more test animals are likely to exhibit toxic symptoms, thus making it easier to identify a causal relationship between the test substance and adverse health effects.

While MTD is conceptually straightforward, it is definitionally complex. The objective is to maximize the sensitivity of the test by finding the largest quantity that can be administered to test animals without interfering with basic biologic processes.[6] That is, if too much of a compound is administered—whether that compound is a pesticide or even food or water—adverse effects can be expected to result because the dosage exceeds the body's ability to manage the excess quantities. Conversely, if MTD is underestimated, and too little of a compound is administered, the experiment may not detect infrequently observed chronic effects.

Officials from several OECD countries told us that their countries, in contrast to the United States, do not place much emphasis on MTD as a tool of risk assessment. Spanish officials said that, when they review data, it is for the purpose of determining the general mechanism of the chronic effect; they do not require that long-term feeding studies be done by administering MTD of a compound. Similarly, officials from Germany's Federal Health Office told us that they follow a "mechanistic" approach to

[5]There has been some recent work using in-vivo bioassays that could accelerate the process of assessing the carcinogenicity of pesticides. Such bioassays would reduce the time and costs needed to do chronic tests. See R. Cabral, T. Hoshiya, K. Hakoi, R. Hasegawa, S. Fukushima, and N. Ito, "A Rapid In Vivo Bioassay for the Carcinogenicity of Pesticides," Tumori, 77 (1991), 185-88.

[6]Blair et al. have noted the inherent difficulty of specifying what MTD "is"; they note that common definitions specify what an MTD "is not." Hence, MTD is defined as the highest dose that does not "(1) alter survival in a significant manner other than tumor production; (2) cause a body weight decrement from concurrent control values of greater than 10 to 12 percent; (3) exceed 5 percent of the total diet, because of potential nutritional imbalances caused at higher levels; or (4) produce severe toxic, pharmacologic, or physiologic effects that might shorten duration of the study or otherwise compromise the use of study results in risk assessment." In S. Baker and C. Wilkinson (eds.), The Effects of Pesticides on Human Health (Princeton, N. J.: Princeton Scientific Publishing Company, 1990), p. 231.

data evaluation—that is, they try to understand the biological mechanisms by which the product produces the observed toxic effects. Chemical company representatives, who prepare and submit registration dossiers to many nations, stated that this approach is common outside the United States.

Discussions at the October 1992 Pesticide Reregistration Workshop in Virginia focused, in part, of this topic. There was general agreement that the dose administered to test animals should demonstrate some toxicity, although there was disagreement about what constitutes a sufficient level. Several participants indicated that their agency may be more flexible in their approach than EPA. Interestingly, only EPA had available documentation that described its process of assessing carcinogenic risk.

Oncogenic Threshold Versus Linear Extrapolation of Cancer Risk

The use of MTD in long-term feeding studies is given greater prominence by EPA because carcinogenic effects are treated differently from other chronic effects. EPA assumes that cancer develops in a way that is qualitatively different from other types of chronic effects. For other toxic endpoints such as birth defects and neurotoxicity, EPA uses a threshold model to extrapolate the level of risk from animal data to humans. Several foreign regulators told us that they do not generally make a distinction between cancer and other chronic effects—a threshold model is used when evaluating data.[7]

A threshold model approach implies that all substances are toxic when administered in quantities that exceed the body's ability to manage them. Thus, an important parameter derived from long-term feeding studies is the dosage at which the compound does not produce toxic effects; this dosage is often referred to as the sub-threshold or no-observed-adverse-effect level. This level is then divided by a safety factor of 100 or 1,000 to determine the "safe" human dose.

EPA does not presume that a threshold exists for carcinogens. Rather, cancer is believed to be caused by an accumulation of damage to a cell's genetic material. In other words, cells become cancerous because they are unable to overcome the cumulative effect of many small traumas. Because EPA believes that a dose-effect threshold cannot be assumed for cancer, it

[7]According to one EPA toxicologist, one reason that regulators in these countries may not pay great attention to MTD in assessing a compound's toxicity is that it is assumed that registrants would want to use the highest possible dose when conducting experiments, since it is this dosage that is subsequently used as a referent in calculating residue standards (that is, how much of a substance can safely remain on a product).

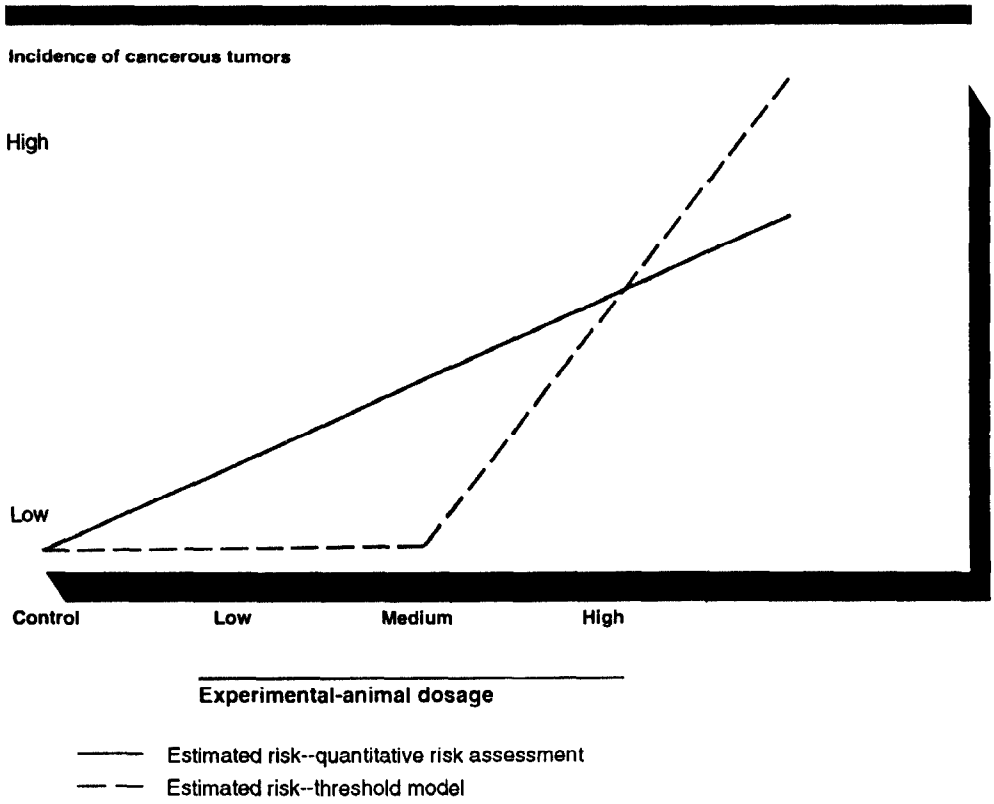
uses a multistage linear model to estimate risk that is often referred to as quantitative risk assessment.[8] This method of extrapolation is regarded by some researchers as conservative because a compound shown to cause cancer at high dosage levels is also assumed to be carcinogenic at lower levels —based on the hypothesis that exposure at any level to a cancer-causing chemical is associated with some increase in the probability of tumor formation.

Using hypothetical data, figure 4.1 provides a simplified depiction of how the two approaches interpret cancer risk. (Actual data may vary depending on the chemical compound.) The broken line represents an estimate of risk that might be obtained from a threshold model. The test substance is assumed to be nonhazardous at control, low, and medium doses; only when administered in high doses is the substance assumed to be carcinogenic. However, under a threshold approach, a safety factor is applied to experimentally tested dose levels to allow for any differences in susceptibility between test animals and humans. The solid diagonal line in the figure is an estimate of the hazard that might be obtained from quantitative risk assessment. As discussed previously, this model posits that, for any level of exposure to a chemical, some risk is posed. Once the dose-effect relationship is established, an estimate is made that describes the potency of the chemical at the 95-percent confidence interval, which is designed not to underestimate the chemical's potency. Although cancerous tumors are observed only in the high dose treatment condition, it is assumed that, given a longer period of exposure, the test substance would also cause cancer under the low and medium dose conditions; hence, even lower dosages present some degree of risk.[9]

[8]EPA uses a safety factor with the no-observed-effect level for some nonquantified class "C" carcinogens—that is, carcinogens with a limited data base suggestive of human carcinogenesis.

[9]Other assumptions regarding extrapolation from MTD are (1) pharmacokinetics are not dose dependent; (2) DNA repair is not dependent on dose; (3) the response is not age-dependent; and (4) a test dose need not bear a relationship to human exposure. "Final Report of the Advisory Review by the NTP Board of Scientific Counselors; Request for Comments," 57 Fed. Reg. 31, 723 (1992).

Figure 4.1: Quantitative Risk Assessment Versus Threshold Model, Using Hypothetical Data[a]



[a]This figure provides a simplified conceptual overview, using hypothetical data to compare these two risk assessment approaches. It does not depict the safety factors that are applied when either approach is used.

The development of quantitative risk assessment for cancer in the United States was heavily influenced by the passage of the Delaney Clause, a 1958 amendment to the Federal Food, Drug, and Cosmetic Act. This amendment prohibited the use in food of any carcinogenic chemical additive that would concentrate in processing. In practice, EPA interpreted this amendment to mean "negligible risk" rather than "zero" risk, thus allowing the registration of pesticides that present cancer risks of less than 1 in 1 million. In so doing, EPA interpreted the Delaney Clause to be more consistent with FIFRA, which allows the balancing of risk and benefit in pesticide registration. In 1992, however, a federal appeals court ruled that the Delaney Clause prohibits EPA from permitting the use of any additive shown to be carcinogenic, regardless of the degree of risk involved. The Supreme Court later declined to hear an appeal by EPA of

that decision. EPA officials subsequently said that they would work to develop new food safety legislation.

The use of MTD and quantitative risk assessment has also been the subject of debate within the U.S. scientific community. The National Toxicology Program (NTP), a part of the Public Health Service under the Department of Health and Human Services, coordinates the toxicology activities of several federal departments: the National Institutes of Health (NIH), FDA, the National Institute of Environmental Health Sciences, the National Center for Toxicological Research, the National Institute for Occupational Safety and Health, and the Centers for Disease Control (CDC). Recently, the NTP Board of Scientific Counselors made several recommendations concerning toxicological research. Specifically, the report of the Carcinogenesis Working Group stated that NTP

"...places too much emphasis on testing per se, and not enough emphasis on providing the mechanistic insight required for a realistic interpretation of the significance of the testing results with regard to human health....Studies directed towards discerning the mechanism(s) of action of the chemical of interest need to be incorporated into, and juxtaposed with, the bioassay in order to place its results into proper perspective."[10]

Clearly, the debate about what constitutes the best approach to assessing carcinogenic risk associated with a pesticide is complex. It also appears that EPA's risk assessment approach and the assumptions that underlie it differ from those of other nations. Several international efforts may shed more light on the significance of such differences. Comparative work on this issue being considered by IPCS is one example. Another example is the comparative data reviews being coordinated by OECD. Such efforts should provide the opportunity to compare and contrast the strengths and weaknesses of these methodologies.[11]

Dietary Exposure Studies

As noted earlier in this chapter, the degree of risk a substance poses to an individual is the product of its toxicity and level of exposure; hence, the risk to a person from a high level of exposure to a moderately toxic substance may, in some instances, be as great as the risk from low exposure to a highly toxic substance. For most persons, diet is the most common route of exposure to pesticide residues. EPA considers two

[10]"Final Report of the Advisory Review by the NTP Board of Scientific Counselors; Request for Comments," 57 Fed. Reg. 31, 722 (1992).

[11]Additional information on the MTD debate can be found in the recent study Issues in Risk Assessment (Washington, D.C.: National Academy of Science Press, 1993).

factors in calculating dietary exposure when establishing tolerances: the amount of a pesticide likely to be in various foods and the quantity of these foods consumed.

The first factor is estimated by using the maximum residue levels obtained from field trial data or the actual residue found in food samples, when such information is available. The second factor is estimated through a survey—called the National Food Consumption Survey—used to determine the type and quantity of food eaten in the United States. The main focus of this survey, which is conducted every 10 years, is to collect information on U.S. dietary patterns, the results of which can be broken down to determine the diet of various subpopulations (such as children and pregnant women) and geographic regions (for example, Northeast, North Central, Southern, Western). Such breakdowns are important since regional diets often differ, as do the food preferences of ethnic groups. Likewise, a typical adult's diet may differ from that of a young child.

EPA compares dietary exposure levels against a pesticide reference dose (RfD). This parameter is derived from short-term toxicology tests (teratogenicity, neurotoxicity) that indicate the expected level of dietary exposure from pesticide use acceptable from a safety point of view.[12]

Officials we interviewed in the course of this investigation indicated that, while dietary studies have commenced in several OECD member nations, this field, at present, is not yet well developed. Several officials noted, however, that EEC regulations due to take effect shortly call for dietary studies, and that they expect that additional testing will be undertaken as a result. (We also learned that efforts are currently under way in the United States to compile a data base containing dietary profiles already completed in many nations.)

Swedish officials told us that they conducted what they termed a limited dietary study in 1985 that focused on the edible parts of fruits and vegetables. In Greece, the paucity of laboratory facilities has constrained the amount of testing that can be done. Consequently, the studies that

[12]For example, let us assume that toxicology studies have determined that it is safe to ingest .5 mg per day of residue from Product X, a fungicide used to prolong the storage life of potatoes, and Product Y, a growth regulator used on Japanese sand pears to control ripening—that is, both compounds are safe so long as no more than .5 mg is consumed per day. Further, assume that the amount of residue in a typical potato treated with Product X is .5 mg and the typical residue in a sand pear treated with Product Y is also .5 mg. Since the typical American is likely to eat more potatoes and food products derived from potatoes (for example, french fries, potato chips) than they are sand pears, Product Y would be safe to use while Product X might not be. Extending this logic to the evaluation process, although both pesticides have the same level of toxicity and are similar in all other respects, disparities in the typical American's dietary exposure to each might result in differing registration decisions.

have been undertaken have focused on a limited number of widely consumed products, such as olive oil. German government documents indicate that that nation first conducted systematic dietary studies in 1988. In Spain, officials said that they had completed one study that looked at pesticides in the major dietary groups and that another project was under way to determine if ADI levels are being exceeded. Italian officials reported that residue levels first began to be monitored in 1991, when the first national dietary studies were undertaken. We found that these nations did not generally take into consideration regional or ethnic differences in diets (although a well-designed survey could be analyzed to assess such differences). In the United States, EPA continues to use data from the 1977-78 National Food Consumption Survey to estimate dietary exposure to pesticides, due to problems with more recently collected data.

In summary, information collected as part of country visits indicates that dietary exposure studies are not yet extensively used in the nations that we visited. This finding has two implications. First, it is likely that dietary exposure information has not figured prominently in the past evaluation decisions of products now on the market in these countries. Second, dietary exposure information is likely to be incorporated into the registration decisions of OECD countries in the future. Given the significant differences in international dietary patterns, as well as the potential of such differences to affect the evaluation of pesticides, it would seem prudent that harmonization discussions address this issue as it pertains to the mutual acceptance of registration decisions.

Risk Management

The decisions of regulators, while guided by the risk assessment process, must also take into account a variety of other factors, including (1) the manner in which the pesticide will be applied, which is determined by what are termed good agricultural practices; (2) the potential benefits accruing from the use of a pesticide; (3) tradeoffs between different types of risks (for example, choosing whether to register a pesticide that may be carcinogenic); and (4) cultural factors that influence the tolerance of risk. Thus, even if it were possible to resolve all methodological and scientific differences of opinion that surround the issue of pesticide evaluation, the process cannot be detached from political and cultural demands. Countries use their pesticide regulatory systems to pursue different ends, and the registration decisions made by one country may not be appropriate for others. This balancing of priorities is often referred to as risk management.

During our site visits to several OECD countries, registration officials pointed out certain risk management philosophies that they believed set them apart from that of the United States. The following section highlights several of these differences.

Efficacy Studies

Efficacy studies are conducted to determine the level at which a pesticide effectively controls pests. In our discussion of registration requirements in chapter 2, we noted that many OECD nations, although not the United States, require efficacy studies.

Although efficacy studies are ostensibly a consumer protection measure—that is, they ensure that the product is effective for the purpose claimed—they can promote health and safety in two ways. First, because it is generally assumed that pesticide residues present some potential risk to the public, efficacy studies ensure that pesticides will not be needlessly used by demonstrating that there is at least some benefit accruing from their use. Second, efficacy studies help reduce pesticide exposure by calibrating the quantity used so that no more of a pesticide is applied to a crop than is necessary to control the target pest. In this way, these studies become an integral part of the risk management process.

In the case of the United States, MRLs are set using a "worst case" scenario—that is, MRL is set to reflect the maximum amount of residue that may remain on a crop. In the process of setting MRLs, EPA does not review product efficacy data submitted by manufacturers. (Efficacy data are reviewed for pesticides used as disinfectants.) Although the United States still reserves the right to request efficacy data from manufacturers, since the late 1970's, submission to, and review of such data by, EPA have not been required for registration. This change in policy is based on the premise that farmers are knowledgeable consumers and that ineffective pesticides would soon be detected in the marketplace. Given the costs involved in developing and testing a pesticide, as well as the potential lawsuits that could result from a defective product, it clearly may not be in the manufacturer's best interest to market an ineffective product.

In contrast, efficacy trials are given more attention in several of the OECD nations we visited. This can result in lower MRLs because regulators are able to determine with more accuracy the amount of residue that should remain on a crop if a pesticide has been applied using good agricultural practices. For example, Germany requires 2-year trials to monitor pesticide use and application.

Sweden has taken an aggressive approach to reducing pesticide application rates by determining the lowest rate possible to ensure crop viability and effective weed control. As part of an effort to reduce pesticide use, Sweden has instituted what is called the "25/50/75" program. This program represents a modified approach to efficacy testing. Rather than determining the quantity of a compound that will kill 100 percent of the pests, this program seeks an 85 percent eradication rate. If 85 percent of weeds/insects are eradicated, yields will not be affected (that is, it is not necessary to kill 100 percent of the pests). Testing is thus performed to determine whether an 85 percent eradication rate can be achieved using 75, 50, or even 25 percent of the recommended dose. Swedish researchers have found that it has been possible to reduce recommended herbicide dosage by one half while returning 75 to 80 percent of maximum herbicidal efficacy.

Reviewing efficacy data as part of the evaluation of pesticides offers the potential advantage of minimizing the amount of the chemicals applied to crops. This would reduce the amount of pesticide residues found on foods, thus decreasing public exposure to them.

Risk Reduction Programs

An outlook gaining attention in some quarters holds that pesticide residues, in any amount, present some level of risk to the public, thus dictating that steps should be taken to reduce the public's overall level of exposure to pesticides. The governments of Sweden, Denmark, and the Netherlands have all introduced extensive pesticide reduction programs. Of these three programs, Sweden's is the oldest and, to date, the most successful.

As initiated in 1986, the Swedish risk reduction program had three elements. The first part called for using pesticides that were less hazardous to health and the environment. This objective was met by phasing out older and unacceptable pesticides that could be substituted for by other pesticides with less hazardous properties. The second part—measures to protect health and the environment—required improved pesticide application equipment and stricter rules for the spraying of pesticides. Additionally, persons who apply agricultural pesticides were required to take a 3-day course in proper application techniques.

The third part of the Swedish risk reduction program called for a 50-percent decrease in the quantity of pesticides used. Between 1986 and

1990, the overall tonnage of agricultural pesticides used in Sweden was reduced by 47 percent compared to the 1980-85 average. This third element in Sweden's program was linked to the use of lower doses of pesticides in the field (one-third reduction). Owing to the success of the 50-percent reduction program, Sweden is now trying to cut pesticide use by another 50 percent.

Reregistration of Existing Pesticides

A major hurdle facing pesticide regulators in the 1990's is the reregistration of pesticides currently on the market. The type and amount of data required to demonstrate the safety of a pesticide expanded considerably during the 1970's and 1980's; thus, those older products still on the market that have not been subjected to today's more scientifically rigorous standards must be reevaluated. Reregistration of these products can play an important part in managing the risk associated with pesticides by removing unsafe products from the market.

Several past studies, including a 1984 study by the National Research Council and the 1987 National Academy of Sciences report, have indicated that the toxicologic information available on many pesticides was outdated and inadequate to meet reregistration requirements at that time. Given the large number of pesticides on the market, reregistration can be a formidable task—both for government personnel, who must review these products, and for manufacturers, who must conduct and pay for studies on compounds for which they may have lost proprietary rights.[13]

Responses we received from American embassy staff indicated that 18 OECD nations have initiated a pesticide reregistration program of some type (although not all provided data on the number of products that have been reregistered). Three countries—Belgium, Iceland, and New Zealand—have not established reregistration programs, and one nation, Australia, is in the early stages of creating one. It should also be noted that the EEC has recognized the importance of reregistering existing pesticides and will initiate reviews of a group of 90 products beginning in 1993. This work will be divided among member states and be done over a 12-year period, which indicates the enormity of the task facing regulatory officials.

[13]In some nations, manufacturers can lose proprietary rights for products that have been on the market for more than a specified number of years. For example, some active ingredients used in pesticides have been sold for many years and may be used in formulations produced by several companies. Because more than one manufacturer is marketing products using the same active ingredient, there is some question about which company or companies should pay for new studies—or whether they all should pay these costs.

We asked what criteria countries use to decide whether a pesticide should be reregistered. Respondents indicated that most countries had one or two measures that triggered reregistration of an older product. The most frequently mentioned reregistration criterion, used by 16 OECD member nations, was that a pesticide be reviewed when new information raises safety concerns about it.

Twelve nations require reregistration of a pesticide after a specified number of years. It was not possible to determine whether this aspect of reregistration is merely a "relicensing" procedure—by which a manufacturer pays a fee to keep a product on the market—or an in-depth evaluation of old studies and any new data generated since registration was first granted. A less frequently mentioned reason for reregistering a compound was that pesticides registered before a certain date must be reregistered; this is the case in seven nations.

Materials we collected on country visits provide additional insight into the reregistration process. For example, Germany grants registration for 10 years and then the product must be reevaluated. German officials reported that some companies do not bother to reregister certain older products because (1) they are aware that these products do not meet current standards, or (2) they do not want to incur the expense of generating the test data required to complete a new registration package for a product with a limited market. The same officials stated that this has had the effect of reducing the number of pesticides registered in Germany by about one third.

In Greece, reregistration occurs every 5 years, at which time the government may request that registrants submit any new studies that have been done on a compound in the intervening period. New data are not always submitted at that point, nor is it required that they be submitted as a matter of course. According to officials involved in product registration, if a problem has been detected, then a more thorough review of the product is undertaken. Greek officials also told us that pesticides that were on the market more than 5 years before the 1977 legislation went into effect are not subject to reregistration, which suggests that older products may not have been evaluated thoroughly.

An Italian official told us that reregistration of existing products was required on a case-by-case basis between 1968 and 1990, usually when a problem with the pesticide was identified. During that period, this senior official said that about 100 of the 300 registered active ingredients had

been reregistered, while approximately 40 had been denied reregistration. Italian officials also stated that legislation requiring reregistration was passed in 1990 and that a deadline of 2 years was set. Since 1990, 20 additional products have been reregistered.

In Sweden, the government has acted to reduce the number of agricultural pesticides on the market. A major step in this process was to declare, in 1986, that the registrations of 450 pesticides registered prior to that year would expire by the end of 1990. Many products would therefore have to be reevaluated if they were to stay on the market. Only 243 of those products were reregistered and approved for continued use in 1991. For 170 products, the manufacturer did not apply for reregistration, and for 52 products, renewal of registration was denied.

The U.S. experience suggests that the reregistration process can be lengthy. Amendments to FIFRA require that EPA generally reregister pesticides containing any active ingredient first registered before November 1, 1984. The U.S. reregistration process is supposed to be completed by 1997. As of the end of fiscal year 1992, 31 of some 20,000 older products had been reregistered. A recent GAO report notes that through fiscal year 1992 the agency had also reassessed the active ingredients used in about 2,370 more products.[14]

As shown in table 4.1, the number of pesticides reregistered in 1991 ranged from zero in Austria, Canada, France, and the United Kingdom to 1,829 in Japan, with most nations reporting having reregistered 100 or fewer of these products. It is likely that reregistration of existing pesticides will expand as the EEC moves toward developing a list of "positive" substances for use throughout EEC member states.

[14]See Pesticides: Pesticide Reregistration May Not Be Completed Until 2006, GAO/RCED-93-94 (May 21, 1993).

Table 4.1: Pesticide Reregistration in OECD Member Countries, 1991

Country	Number of pesticides reregistered in 1991[a]
Austria	0
Canada	0
France	0
United Kingdom	9
United States	31[b]
Greece	11
Italy	14
Finland	16
Ireland	20
Norway	29
Denmark	39
Portugal	45
Turkey	81
Germany	100[c]
Sweden	243
Japan	1,829

[a]Australia, Belgium, Iceland, and New Zealand do not currently have reregistration programs. We have listed information only for countries for which we have received complete responses. These figures refer to pesticide products.

[b]This figure is as of the end of fiscal year 1992. Through fiscal year 1992, EPA had also reassessed (but had not reregistered) the active ingredients used in about 2,370 more products.

[c]The respondent indicated that this figure is an estimate.

Groundwater Studies in Europe

Another way of reducing the risk associated with a pesticide is to limit the amount released into the environment. One topic repeatedly raised in conversations with us by industry representatives and government officials in European nations was the strict EEC rule concerning pesticides in groundwater. Currently, the amount of residue permitted is 1 part per billion per liter, or what one regulatory official described as "0" tolerance. One industry official lamented the difficulty of meeting such an exacting standard, and government officials in Greece noted the potential difficulty of enforcing such standards. This is especially true in Greece, where the lack of proper equipment currently precludes testing.

To determine whether a pesticide can reach groundwater, soil studies are commonly required. One of the most difficult of these tests has been

developed by the German government. Referred to as a lysimeter study, it consists of monitoring a large section of soil to determine leaching characteristics.

Summary

This chapter compared the United States with other OECD countries on two dimensions that relate to the evaluation of pesticides: risk assessment and risk management. With regard to risk assessment, we found that EPA applies a scientific model to assess the carcinogenic risk that is different from those used in other countries. Although we did not find additional instances of scientific disagreement over other types of toxicological effects (for example, reproductive toxicity), neither can we confirm that they do not exist. The lack of procedural transparency in the evaluation process of OECD countries made identification of such differences problematic. We note that the EEC has prepared detailed draft documents outlining standardized guidance for date reviews, a measure that should facilitate transparency among its member states.

With regard to risk management, we found that the registration decisions of OECD countries are sensitive to national priorities. This finding, while not precluding the possibility of greater harmonization of registration standards, raises doubts about the interchangeability of national registration decisions at this time.

Enforcement and Monitoring of Pesticide Standards

Introduction

In this chapter, we address our final evaluation question, "What measures are used to enforce pesticide standards in OECD nations, and how do they compare with those of the United States?" All of the 22 OECD nations that completed our survey indicated that they have systems in place to test and evaluate samples of food for pesticide residues. However, in the course of analyzing survey responses and conducting case studies, we found that enforcement efforts and capabilities vary among OECD nations. In four of the five countries that we visited, enforcement is not centrally coordinated; rather, it is handled by local or regional authorities. In addition, we found that enforcement efforts are primarily focused on food imports; resources in fewer nations are devoted to monitoring exports and, to a lesser extent, domestically grown and consumed foodstuffs.

There are several imminent changes that will have significant implications for enforcement activities in Europe. Specifically, EEC member states are slated to improve their enforcement activities in accordance with several directives scheduled to take effect in 1993. In light of the goal of having free movement of goods in the EEC, such activities will have an important role in assuring that food safety standards are upheld.

The enforcement side of a pesticide regulatory system can also have serious trade implications, especially when a country does not permit residues from a pesticide to appear on or in food imports. During our country visits, pesticide regulatory officials brought several such incidents to our attention. In one instance, Greek officials noted that a shipment of peppers had been denied entry into the United States by FDA because it contained residues of a pesticide that has not been registered or granted an import tolerance by EPA. The officials pointed out that MRL had been established for the compound by other European nations and that the amount of residue detected was below that level, raising a question in their minds as to whether FDA was using the lack of MRL as a trade barrier in this case.

Enforcement Standards: an Overview

As discussed in the preceding chapters, in order to make decisions about a pesticide's safety, regulatory officials review and evaluate a range of test data submitted by registrants. One objective of this review is to determine legal limits for residues that permit a pesticide to be used without posing unacceptable health or environmental risks. The measure that is established is referred to as a tolerance in the United States, and as a maximum residue limit (MRL) in other nations. A tolerance is the maximum level of pesticide residue legally permitted to remain in or on a crop in

commerce—it is a key factor in any pesticide residue control system. If the residue level on an agricultural commodity exceeds this limit, the commodity can be refused entry into U.S. commerce.

Twenty-one of 22 survey respondents indicated that MRLs are established for active ingredients used in pesticides; the one nation that does not establish MRLs is Iceland.

Banned or Severely Restricted Products: Trade Implications

If the risks associated with a pesticide are deemed unacceptable, a regulatory agency may suspend, cancel, or restrict its use. We found that 20 of the 22 OECD member nations maintain a list of pesticides whose use has been banned.[1] We also found in the course of our country studies that products that have been banned or severely restricted by one nation may be judged acceptable by another. This circumstance has created tension between southern European nations, where large quantities of fresh fruit and vegetables are grown for export, and northern European nations, which import these crops but have more restrictive regulations concerning pesticides (and less need for some pesticides due to different ecological conditions). In the course of our interviews with officials in several OECD nations, this issue arose several times. In Spain, both industry representatives and government officials noted that Spanish agricultural producers sometimes encounter difficulties exporting commodities because pesticides approved for use in Spain have been judged unacceptable by other countries. Within a particular regulatory system, other apparent contradictions sometimes exist. For example, Swedish officials have established an import tolerance for carbendazim (an unregistered pesticide produced in and exported from the United States) even though that product's use has been severely restricted by KemI, the Swedish Chemicals Inspectorate, which sets such measures. In this case, the pesticide, although hazardous, was deemed acceptable on foods because consumers may safely be exposed to small amounts of its residues over their lifetimes.

Acceptance of Other Nations' Standards

In international agricultural trade, instances may arise in which a country has not established a MRL for a pesticide or the pesticide may not be registered for domestic use, but its residues are nevertheless detected on imported foods. In such cases, the country may refuse to allow the product

[1]In the United States, EPA can suspend registration of a pesticide to prevent an imminent hazard to health or safety. It can cancel registration if the product may cause unreasonable adverse effects or its risks outweigh its benefits, as well as for noncompliance with FIFRA. A manufacturer may voluntarily cancel registration of a product if, for example, adverse health or safety data come to light.

onto the market. U.S. policy, for example, is to detain or return such products if EPA has not registered the pesticide or set an import tolerance.

We asked all OECD nations if their enforcement policies included accepting other nations' MRLs, or those of international bodies such as the Joint FAO/WHO Codex Alimentarius Commission.[2] We found that five nations—Canada, Iceland, Japan, Turkey, and the United States—reported that they do not accept other nations' MRLs or those established by Codex. Other nations will consider Codex-established MRLs or those of other nations if they have not established their own MRL for a pesticide. (See table 5.1.)

Table 5.1: Pesticide Standards Considered by OECD Member Nations[a]

Standards accepted	Countries
Codex standards	Australia, Belgium, Finland, Greece, Ireland, Norway, New Zealand, Sweden, United Kingdom
Exporting nation's MRL	Finland, Sweden, United Kingdom
EEC directives	Belgium, Denmark

[a]Responses listed are those with complete data. Respondents noted that they may consider these other standards if they have not established one themselves.

Survey respondents from several OECD countries indicated that acceptance of nondomestic standards is done on a case-by-case basis. As shown in table 5.1, nine nations will consider MRLs established by Codex. Three nations reported that they will consider an exporting nation's MRL, and two nations will consider standards determined by the EEC. These findings highlight the extent to which Codex standards can potentially serve as reference points when government officials in OECD member nations make judgments about pesticides they have not reviewed or approved. These findings also underscore the flexibility of different nations in accepting an assessment made by another nation or an international group when they themselves have not evaluated a product.

[2]The Codex Alimentarius Commission is a subsidiary body of the Food and Agriculture Organization of the United Nations (FAO) and the World Health Organization (WHO). The Commission is frequently referred to as "Codex," which is involved in numerous activities related to facilitating world trade in foods and internationally accepted standards. Part of the Commission's work falls under the Codex Committee on Pesticide Residues, which has established over 2,000 MRLs based on advice from an expert committee. These MRLs represent a consensus of international opinion about the safety and practicability of a wide range of pesticides. See our report entitled International Food Safety: Comparison of U.S. and Codex Pesticide Standards, GAO/PEMD-91-22 (August 22, 1991).

Enforcement and Monitoring Methods

In monitoring and enforcing residue standards, countries typically strive to meet several different objectives. These span such activities as checking to determine whether established MRLs are being followed and testing fields or crop shipments to determine whether MRLs are being exceeded and thus enforcement action is required. We devoted several survey questions to determining what types of methods OECD member nations use to monitor compliance with pesticide regulations. Information on these practices is presented in table 5.2.

Table 5.2: Monitoring and Enforcement Methods Used by OECD Nations

	Monitoring and enforcement methods		
Country	Testing food shipments	Observing field applications	General use data[a]
Belgium	•	•	•
Canada	•	•	•
Netherlands	•	•	•
Germany	•	•	•
Finland	•	•	
Australia	•	•	
New Zealand	•	•	
Spain	•	•	
Sweden	•	•	
Italy	•	•	
United States[b]	•	•	
Greece	•		•
Denmark	•		•
Portugal	•		•
Ireland	•		
Norway	•		
Japan	•		
France	•		
Iceland	•		
United Kingdom	•		
Austria	•		

[a]Includes sales reports and/or reports of professionals specializing in pesticide application.

[b]In addition to the methods listed, the United States also inspects production and distributor facilities, monitors test data validity and checks on good laboratory practice standards, and develops establishment-registration and annual-production reports.

The most frequently cited monitoring method was testing samples of food shipments for pesticide residues (21 nations). Other common monitoring methods were conducting observations of field application of pesticides (11 nations) and monitoring general pesticide use data, such as sales figures or reports of professionals specializing in pesticide application (7 nations).

Monitoring activities reported only by the United States included inspecting of production and distribution facilities, checking on data validity of residue testing equipment by insuring compliance with good laboratory practice standards and performing data audits, and producing establishment-registration and annual-production reports. Officials we interviewed during our country studies indicated that there is little work done along these lines in their countries. In some cases, such as Sweden's, few pesticides are manufactured in the country, so monitoring of production facilities is not necessary. Other nations, such as Greece, import the active ingredients, which are then used to make the formulated product. The Greek government has started to collect statistics on production and use, and a British market research firm has published a document that outlines the status of the chemical industry. Spanish officials said work is under way to assess the status of plants that manufacture pesticides; other information on pesticide use, production, and distribution is published by the industry trade association. In Germany, the Laender (regional governments) are responsible for monitoring the shipment of pesticides, providing advice to farmers about their use, testing application equipment, and conducting surveys and trials.

Testing of Crop Shipments for Residues

Because sampling crop shipments is the most common pesticide monitoring activity, our survey also asked which types of product shipments are sampled. As shown in table 5.3, 21 nations reported that they have programs to test imported and domestic products for pesticide residues. Thirteen countries monitor exported foods, and 18 monitor domestically grown products for residues.

Table 5.3: Types of Agricultural Shipments Sampled in OECD Nations

	Type of product sampled		
Country	Imported	Exported	Domestically grown and consumed
Australia	•	•	•
Belgium	•	•	•
Canada	•	•	•
Finland	•	•	•
Greece	•	•	•
Italy	•	•	•
New Zealand	•	•	•
Spain	•	•	•
Sweden	•	•	•
Ireland	•	•	•
Germany	•	•	
Portugal	•	•	
Austria	•		•
Denmark	•		•
France	•		•
Iceland	•		•
Japan	•		•
Netherlands	•		•
Norway	•		•
United Kingdom	•		•
United States	•		•

Enforcement Actions

As noted previously, OECD nations take different approaches to monitoring and enforcing pesticide regulatory standards. In this section, we discuss survey responses and data collected while carrying out our country studies that help highlight these differences.

In Sweden, the National Food Administration's 250 staff members enforce pesticide residue standards, and Sweden has sampled between 4,000 and 5,000 food shipments annually since 1972. The officials we interviewed emphasized the importance placed on enforcement efforts because an estimated 80 to 90 percent of the country's fruit is imported. They also noted that approximately 75 percent of the sampling done is on imports.

Swedish officials also explained the different enforcement strategies they use. One strategy is to over-sample food shipments that they believe may have higher residue levels. Such decisions are based on prior experience and information provided by other nations, especially other Nordic countries with which they regularly exchange such data.

Swedish enforcement efforts also utilize a three-pronged regulatory monitoring strategy, whereby a crop with residues in excess of an MRL may be permitted on the market but subsequent shipments from the same source are monitored closely.[3] The second level of enforcement is termed compliance monitoring, which involves sampling the next five consecutive lots of the same crop from the same shipper to determine whether they contain violative residue levels. The third level of monitoring involves blacklisting or banning imports of the crop from the same shipper if violative samples continue to be found.

Germany's monitoring system for pesticide residues on foodstuffs was established relatively recently, in 1988. It operates under the auspices of the Federal Ministers for Health and for Research Technology, with the Federal Health Office overseeing work done at 36 official food inspection laboratories operated by the Laender. Documentation provided on these efforts notes that 9,000 food samples were analyzed during the initial 18 months of testing, utilizing EEC-harmonized sampling procedures.

The Italian Ministry of Health has primary responsibility for monitoring compliance with pesticide standards. Monitoring is carried out by local units of the public health service, of which there are 600 throughout the country. The Ministry does not require the local units to report the results of their monitoring activities, although such reporting does occur on a voluntary basis. Officials estimated that, in 1991, 3,000 to 4,000 crop samples were drawn and tested throughout the country, and an estimated 5 to 6 percent were in violation of residue standards. In an effort to strengthen monitoring and enforcement, the Italian government in early 1991 began requiring farmers to keep a "country diary"—a record of every pesticide application. Farmers were subject to a fine if they did not keep the diary. The farmers protested vehemently and disregarded the requirements. As a result, the government delayed enforcement for 2 years.

[3]Swedish officials said that crops with residues in excess of MRLs sometimes remain on the market because the results of laboratory tests may not be available until after a shipment has left the customs area. The crop thus goes into the marketplace with violative residues, but subsequent shipments of the crop from the same shipper are monitored closely.

Greek regulatory officials noted that there is currently only one laboratory in the country. While there are plans to construct additional laboratories to analyze crop samples, funding to build them has not yet been approved. At present, local government prefectures are charged with enforcement, and they send samples to be tested to the Benaki Institute, which is located in an Athens suburb. There is no government-sponsored effort to collect data on usage patterns.

In Spain, officials in Madrid reported that 90 percent of the enforcement work is done by the nation's 17 regional governments. Enforcement and monitoring data are not compiled or analyzed across the different regions by central government authorities. Regulatory officials did say that the EEC directives scheduled to go into effect in 1993 will bring about change in this aspect of the Spanish enforcement system.

A government representative explained that enforcement of pesticide standards in Spain is often accomplished through private means. That is, because fruit and vegetable exports are important to Spain's economy, exporters often sign contracts with growers that mandate which pesticides can be used on crops and stipulate acceptable agricultural practices, such as application intervals and methods. Compliance with an importing nation's standards is thus more likely, and the possibility that produce will be rejected by the importing nation is minimized. Similar contractual arrangements are also reportedly common between food producers, brokers, and food processors in the United States.

In the United States, EPA establishes tolerances, and FDA monitors and enforces compliance with these levels—with the exception of those for meat and poultry, which are the responsibility of the U.S. Department of Agriculture (USDA). In fiscal year 1991, 19,082 samples—18,214 as part of surveillance and 868 for compliance—were analyzed under regulatory monitoring in the United States, according to FDA's pesticide program publication Residue Monitoring, 1991. Of these samples, 8,466 came from domestic products and 10,616 from imports. In fiscal year 1991, no violative residues were found in nearly 98 percent of the import surveillance samples and 99 percent of the domestic surveillance samples.[4]

[4]A recent GAO report found that some U.S. food imports that contain prohibited pesticides are entering into commerce. This is occurring because importers have not returned some adulterated shipments to Customs for supervised export or destruction. See Pesticides: Adulterated Imported Foods are Reaching U.S. Grocery Shelves, GAO/RCED-92-205 (September 24, 1992).

Summary

Enforcement of pesticide residue standards is an area fraught with potential conflicts. On the one hand, regulatory officials must safeguard public health by ensuring that foods containing unsafe residues do not enter into commerce. On the other hand, enforcing residue standards may lead to charges that a nation is using such standards as a nontariff trade barrier. Perhaps as a concession to the latter concern, many countries showed some flexibility in enforcement of standards. For example, some countries would accept (or consider accepting) a MRL standard developed by another nation or by Codex, if one had not yet been domestically established.

In the course of our visits to five EEC countries, we found that pesticide residue standard enforcement efforts are generally not centrally coordinated; rather, they are administered by local or regional authorities. In the case of one nation, enforcement capabilities are virtually nonexistent due to a paucity of residue testing equipment. Survey data showed that enforcement mechanisms in OECD nations are mainly directed toward food imports, with resources in fewer nations being devoted to monitoring exported commodities and domestically grown and consumed foodstuffs.

Summary and Conclusions

In this chapter, we summarize information that has been presented on each of our evaluation questions and then conclude with a section on matters for congressional consideration.

Data Requirements for Registering a Pesticide in an OECD Nation

The discussion in chapter 2 addressed our first evaluation question, which asked about the experimental test data required to support registration of food-use pesticides in OECD member nations and how these requirements compare with those of the United States. The information presented in matrix form in this chapter should help inform U.S. and international officials at organizations such as OECD as they discuss harmonizing registration requirements. It may also be useful to compare it with a similar study of requirements completed by OECD in early 1993.

Across the 18 OECD nations for which we obtained documentation on registration requirements for food-use pesticides, we found broad agreement on the two sets of toxicology tests used to assess human health effects (acute and subchronic toxicity tests), with less standardization of subchronic tests. With regard to environmental and wildlife test requirements, we found less agreement across nations. This can be attributed to the different ecological conditions found in each country, as well as to differing national concerns. We also found that OECD nations generally place emphasis on reviewing pesticide efficacy data, while EPA does not require such data for most pesticides.

Although there was broad consensus with regard to the range of toxicology studies required to support a registration application, the areas of disagreement, however minor, raise questions that EPA officials should explore further in order to determine their significance, especially in light of the agency's interest in harmonizing these requirements. While environmental and wildlife testing may be difficult to standardize given the ecological variation that exists across nations, such studies can be extremely important in determining the overall safety of a pesticide.

Organizational Structures

Our second evaluation question asked about the organizational structures OECD nations have in place to evaluate pesticides. To answer this question, we relied primarily on data collected during our country visits. We found that the size of the staff responsible for conducting data evaluations varied significantly among these countries. Likewise, the number of pesticides that nations have reviewed and registered, which is discussed in chapter 3, highlights the disparate amount of work facing OECD nations. Although

countries with small staffs can and do rely on advisors from universities or similar organizations to assist in the review process, it is unclear to what extent this helps to overcome staffing disparities.

Data Evaluation and Risk Assessment Procedures

Our third evaluation question asked about risk management and risk assessment procedures followed to evaluate test data in OECD nations. While test data submitted in support of registrants' application dossiers play a crucial role in shaping decisions about the safety of a pesticide, how these data are evaluated by regulatory officials is also important. When conducting our country studies in five nations, we found methodological and other differences that have implications for the process of evaluating test data.

With regard to evaluation methodology, we noted that carcinogenic risk assessment procedures followed in the United States by EPA differ from those followed in other OECD countries. For carcinogens, the United States uses an approach that assumes accrued probability to estimate cancer risk, whereas other OECD countries use a threshold approach. This difference of approach has implications for how cancer risk is estimated and, accordingly, the types of pesticides that may or may not be granted registration. Such differences are important and have been the subject of ongoing debates within the U.S. and international scientific communities.

The United States also differs from other OECD countries with regard to the transparency of its evaluation process. In the United States, decisions rendered by regulatory authorities are recorded and made publicly available, and thus it is possible to determine the relative importance of the various components of the data package. We found that final registration decisions in OECD countries we visited were made by review panels that were not required to provide a written rationale for their decision. It is thus difficult to determine whether the criteria used to evaluate pesticides are equivalent across countries. Similarly, the United States has developed guidelines to aid scientists engaged in the risk assessment process, an area that appeared to be less well developed abroad—although important changes in this area are expected for EEC nations in 1993.

The process of evaluating information and assessing risks is also driven by cultural and political factors. The level of risk deemed appropriate varies among nations, as does the need for the use of pesticides on crops. We found that several nations have undertaken programs to manage risk by

reducing pesticide availability and use. As discussed in chapter 4, some of these efforts to reduce risk occurred when nations reevaluated existing products to ensure that they met current standards. Reregistration of existing products, an area where EPA has experienced considerable delays, is an important aspect of managing risk because older, unsafe products are often removed from the market in the process.

Enforcement Measures

Our fourth evaluation question asked about measures used to enforce pesticide standards in OECD member nations. We found that there was some flexibility in enforcement standards, with pesticide MRLs established by the Codex serving as a reference point for some nations in which a national standard has not been established. However, several nations, including the United States, do not accept other standards.

With regard to enforcement measures, we found that the scope of these efforts varied considerably across nations. Three of the five nations we visited—Germany, Italy, and Spain—have relatively new, decentralized systems; in Spain, we also found that enforcement information was not centrally compiled or monitored. Greece has little residue monitoring capabilities at this point, having only one laboratory with the appropriate equipment to do such testing. Sweden has a centrally run program that conducts a variety of residue tests, focusing primarily on food imports.

Harmonization Issues

In the course of our work, we found widespread interest in harmonization issues. Considerable work was under way in the EEC to harmonize both data requirements and evaluation procedures. Because EEC members are also part of OECD, and directives regarding harmonization are expected to be in place in these nations by July 1993, there is major potential for change in European pesticide registration procedures. Important aspects of the EEC plan include working toward developing a list of products acceptable for use throughout the EEC and a reregistration program that will review currently registered pesticides using current standards.

OECD has played an important role in developing the international regulatory framework. One key contribution has been to develop the widely used and accepted Guidelines for the Testing of Chemicals. Ongoing work to update this volume could lead to a set of common "core" data requirements, a goal that should be within reach in light of our previously discussed finding about data requirements.

Country officials and industry representatives we interviewed also expressed their support for harmonization. There is, however, concern about the shape harmonization could take. The pesticide industry feared that harmonization might result in the most stringent regulatory standards, which could be difficult to meet. Conversely, some regulatory officials we interviewed were concerned about the possible dilution of standards—that is, that less stringent standards might be adopted. There was also some concern that harmonization could result in rigid standards that would be difficult to change in order to keep pace with scientific advances.

Matters for Congressional Consideration

International efforts to harmonize pesticide regulations have several objectives, including minimizing trade difficulties among nations while maintaining health and environmental safety. If the Congress wishes to address the implications of U.S. participation in harmonization, then the present study raises several issues that need to be considered.

With regard to data requirements, there appears to be general agreement about human toxicology test requirements but less accord on environmental testing. Ongoing OECD efforts to standardize data requirements should further reduce differences among nations. We also found important differences in the size of the staffs different nations consider necessary to review data packages. This means that even if there are agreements among nations about what needs to be reviewed, the review itself may be very different given the major disparities between countries in the resources available for such reviews.

There is less agreement in other areas. With regard to data evaluation procedures, there is notable variation across nations in the approaches followed. Such differences in evaluation procedures are somewhat obscured by a larger issue—the need for transparency in the decision-making process surrounding pesticide registration. Until this issue is resolved, it will be difficult to determine the extent to which decisions made by different nations are in fact comparable. This also means that there may be more real differences between nations in decision-making procedures than are currently apparent. In terms of how residue standards are enforced, this report has also pointed out areas where some differences in approach and resources exist among OECD nations.

We found that several fundamental differences exist in the pesticide regulatory systems of OECD nations. Although at this time these disparities are too great to warrant taking what may be the final step in broader pesticide harmonization—recognition and acceptance of other nations' registration decisions—further work should be conducted to clarify these differences. The Congress thus may wish to encourage EPA to expand its present efforts to include a more in-depth review of these differences in order to determine what resolutions are possible.

Methodology Used to Code OECD Data Requirements

The material describing data requirements we received from OECD countries varied markedly in comprehensiveness, level of detail, and terminology. Several countries provided a cursory outline of the tests required to register a pesticide, while others provided monographs that described not only test requirements but also portions of the recommended test protocol (for example, the type of animal to be used in the experiments, the number of test replications, and method for reporting test results). It was not possible to determine whether the differences in the quality of documentation that we were provided reflect the level of sophistication that a country's pesticide regulatory program has attained, or whether these differences are due to the fact that additional relevant documentation was not given to American embassy staff. Such differences nonetheless meant that we had to perform our country-by-country comparison of test requirements at a more general level.

Limitations of Coding Scheme

In coding the registration guidelines of OECD countries, it was our intent to follow the test requirements for food-use pesticides outlined in the 1991 edition of the Code of Federal Regulations as closely as possible. Unfortunately, the lack of uniformity in the materials we received from several OECD countries prevented us from coding several types of test requirements at the same level of detail as those contained in the Code of Federal Regulations.

U.S. standards differentiate between "required" and "conditionally required" tests. According to EPA, data designated as "conditionally required" must be submitted if warranted by a product's "use pattern, physical or chemical properties, expected exposure of nontarget organisms, and/or results of previous testing."[1] Because the "required" versus "conditionally required" distinction was not uniformly present in the information we received from OECD countries, it was not possible to incorporate this attribute into our coding scheme.

Although we initially believed that the "conditional/required" dimension might shed light on which types of tests a country considers most critical to the evaluation process, in our review of guidelines that did contain this information, we found little variation between countries. Moreover, through interviews with regulatory officials, we learned that the exact test regimen that a country may ultimately require before granting registration cannot be deduced solely from written guidelines. That determination is

[1] 40 C.F.R. sec. 158.101 (1991).

dependent on a product's attributes and the judgments of the scientists engaged in its evaluation.

A second attribute that we were not able to incorporate into our coding scheme pertains to the test substance. U.S. guidelines differentiate between tests performed on the active ingredient and tests performed on the formulated product. An active ingredient is a chemical compound that acts on the target population (that is, kills pests, regulates plant growth, or defoliates), whereas a formulation is the substance that is commercially sold and contains the active ingredient plus other agents (for example, solvents, emulsifiers, water). Although the registration materials of many countries did specify which tests were to be performed on the active ingredient and/or the formulated product, once again the lack of this information for all countries precluded including this attribute in our coding scheme.

Variations in Test Protocols

An aspect of a country's test regimen not adequately captured by taking a simple inventory of data requirements is the test protocol under which studies are conducted. Formalized test protocols specify the minute details of the experiment—for example, the number, age, and species of animals to be used in the experiment, as well as the dosage of the test substance to be administered. While the test protocols developed by EPA and OECD are perhaps the most extensive and widely accepted, OECD countries have, to varying degrees, developed their own test protocols. To convey a general sense of the range of variation present in these protocols, we present in table I.1 a comparison of three guidelines (Canadian, German, and U.S) that was prepared by Groupement International des Associations Nationales de Fabricants de Produits Agrochimiques (GIFAP), an international organization that represents chemical manufacturers. This table describes how one data requirement, the aqueous hydrolysis study, should be conducted. In the United States, this type of study is part of the environmental fate data requirements and is used to assess how rapidly a pesticide will decompose in water.

Table I.1: Comparison of Guidelines for Aqueous Hydrolysis Studies

	Origin of guideline		
Requirement compared	**United States**	**Canada**	**Germany**
When required	Obligatory	Obligatory	Obligatory
pH of Water	5,7,9 acetate or borate buffers recommended; phosphate buffer not recommended; check on buffer effects required	5,7,9 buffers not specified; information on possible buffer catalysis effects required	5,7,9 ± 0.2 buffers proposed, including a phosphate buffer
Sterility	Sterile conditions required	Sterile conditions required; proof of sterility required	Glassware to be heated to 180°C; buffers boiled for 20 minutes
Concentration	Up to 250 ug ml^{-1}	Dilute solution	≤ 100 ug ml^{-1}
Temperature	25°C ± 1°C	20° or 25°C	22°C or at least two higher temperatures
Sampling	Sample during two half-lives, but usually no longer than 30 days; sample at least 6 intervals between 20-70% hydrolysis, or 15-20% for compounds that hydrolyse slowly	Sample up to half-life plus one further interval, but not more than 30 days. Sample at least 6 intervals	Number of sampling intervals not specified, but study need not exceed 30 days
Number of samples at each interval	Duplicate	Duplicate	Duplicate
Cosolvent	Use only water if possible, but up to 1% of a cosolvent is allowed.	Use only water if possible, but up to 1% of a consolvent is allowed	Maximum permitted concentration is 1%
Identification of hydrolysis product	Any product generated at >10% to be identified	Any product generated at >10% to be identified	Required
Preliminary study	Not accepted	Not accepted	Not considered

Source: GIFAP, Uniform Principles: Data Guidelines and Protocols (Brussels: 1991), pp. 94-5.

As shown in table I.1, though many aspects of the test protocols recommended by Canada, Germany, and the United States are identical, certain features are unique to each country. While the rationale behind certain country-specific requirements is logical and to be expected—Canada, for instance, has a colder climate and thus requires that this test be conducted at lower temperatures—other differences appear to have no obvious explanation. For example, with regard to the kind of water used in this study, Canada recommends distilled water, Germany double-distilled water, and U.S. guidelines do not specify water purity save that the water used should be free of all live bacteria.

Are Studies Equivalent?

The minor procedural deviations illustrated in table I.1 beg the question, Do such differences matter? This question can be addressed from either a scientific or practical standpoint. With regard to the former, it cannot be disputed that altering any one element in the experimental protocol will result in a different experiment. In the foregoing comparison, the German study conducted at 22°C is technically not the same as the American study conducted at 25°C, yet is a temperature difference of 3°C of sufficient magnitude to produce results that would lead to disparate conclusions? It is beyond the scope of this report to provide a definitive answer to this question; however, we learned in our country studies that, as a practical matter, registration systems allow registrants some latitude in presenting test results.

In discussions with agency staff, we were told that EPA does not assert that its suggested protocol is the only proper and valid way to conduct a study. Rather, while studies conducted in accordance with EPA guidelines will not be rejected on methodological grounds, studies generating data through the use of other test protocols (for example, OECD's) may also be acceptable.[2] Further, agency staff said that some of the fine details specified in EPA guidelines are not necessarily essential to conduct a valid study, but were developed in response to questions from registrants who sought a standardized way of fulfilling test requirements.

[2]In discussions with EPA staff, we were told that a data package is evaluated in its entirety, and if a methodological question arises with regard to a particular test, EPA may require that the test be redone to correct the flaw.

Unregistered Pesticides Exported From the United States

Background

We contacted U.S. pesticide manufacturers to determine what types of data they had submitted to register their products in different OECD countries. The pesticides at issue were those manufactured in and exported from the United States, but not registered here. It was our intent to collect information on actual data submissions that would complement the information on test requirements (obtained from registration guidelines) presented in chapter 2. Although our request sought information on a narrow range of compounds, such data had the potential to illuminate a crucial regulatory issue—that is, to what extent are the data requirements listed in the guidelines of OECD countries reflective of the types of data that are received by OECD countries for review? In other words, do OECD countries receive the types of test data they require?

To obtain information on actual data submissions, we constructed a data collection instrument based on the 1991 edition of the Code of Federal Regulations. Among the items included in this instrument were questions that solicited information on the type of test data submitted, the guidelines (EPA, OECD) followed, and the laboratory that generated the data. We also asked about the following types of studies that are typically requested to support registration petitions (and are listed in the tables in chapter 2): specific chemical identity and residue tests; the complete range of toxicology tests (acute, subchronic, chronic); environmental and wildlife studies; general metabolism, dermal penetration, and domestic-animal safety tests; worker reentry protection, spray drift, and beneficial insect studies; and efficacy tests. We also asked for information on ADIs and MRLs that Codex and other nations may have established for these products.

We contacted six U.S. manufacturers of unregistered pesticides and asked that they list the different tests they submitted to register 10 pesticides in 1 or 2 OECD nations. (See the following section of this appendix for a description of the sampling method used.) Company representatives responded by requesting that we work through an intermediary, the National Agricultural Chemicals Association. After several months of discussions with association officials, we arranged two roundtable meetings with industry representatives to discuss both our request and general issues pertaining to registration in OECD countries. With one exception, U.S. pesticide manufacturers declined to provide information on test data submitted to obtain registration in OECD countries.

In the absence of corroborative data of the type we requested from these U.S. manufacturers of unregistered pesticides, we were unable to determine the extent to which the test requirements listed in guidelines of

OECD countries correspond to the range and types of test data submitted to, and reviewed by, these countries.

Selected Information on U.S.-Unregistered Pesticides, 1990

We determined that in 1990, the most recent year for which complete FIFRA section 17 export data were available to us, there were 47 pesticides manufactured in and exported from the United States that appeared to be subject to the proposed legislation (S. 898 and H.R. 2083).[1] Because our objective was to gather information on products that could be used on food and that had not been evaluated by EPA, we excluded compounds that (1) had a U.S. food tolerance, (2) had a registration that was cancelled by EPA, (3) had nonfood-use applications (for example, rodenticides), or (4) were no longer manufactured in the United States. In addition, we excluded several products from the initial list that had been granted a U.S. registration since the 1990 data were compiled. Using these criteria, we excluded 30 compounds, resulting in a set of 17 unregistered pesticides. (See table II.1.)

[1]According to section 7 of the Federal Insecticide, Fungicide and Rodenticide Act, as amended (92 Stat. 829), all registered pesticide-producing establishments must submit a report to EPA by March 1st of each year.

Table II.1: Selected Information on 17 U.S.-Unregistered Pesticides

Compound	Use[a]	Number of OECD registrations	Number of basic producers[a]	U.S. registration pending?	Banned in any OECD country?[b]	Manufacturer
Alphamethrin	Insecticide	11	2	No	No	FMC
Butachlor	Herbicide	1	12	Yes	No	Monsanto
Cadusafos	Nematicide/ insecticide	2	1	No	No	FMC
Carbendazim	Fungicide	13	13	Yes	No	DuPont
Carbosulfan	Nematicide/ Insecticide	9	1	Yes	No	FMC
Esprocarb	[c]	0	1	No	No	ICI
Ethametsulfuron methyl	[c]	4	[c]	Yes	No	DuPont
Flusilazole	Fungicide	9	1	Yes	No	Dupont
Haloxyfop	Herbicide	9	1	Yes	No	Dow
Ipsdienol	[c]	0	[c]	No	No	Bedoukian
Nuarimol	Fungicide	12	1	No	No	Dow
Prosulfocarb	[c]	4	[c]	No	No	ICI
Prothiophos	Insecticide	2	1	No	No	Miles
Simetryn	Herbicide	0	1	No	No	Ciba-Geigy
Tebuconazole	Fungicide	5	2	Yes	No	Miles
Terbumeton	Herbicide	8	2	No	No	Ciba-Geigy
Thiometon	[c]	13	1	No	No	Miles

[a]Farm Chemicals Handbook (1992).

[b]United Nations Environmental Program—International Registry of Potentially Toxic Chemicals, "Report on Chemical Substances Banned or Severely Restricted."

[c]Not available.

From the set of 17 compounds, we randomly selected a subset of 10 products. These 10 products are manufactured by 6 different companies. Since some of the products selected are registered in up to 13 different OECD countries, we requested information from manufacturers regarding what test data they had submitted to register the product(s) in 1 or 2 of these nations.

Background Information on Unregistered Pesticides

As noted previously, although information about the types of test data that had been submitted to OECD nations in support of registration was not provided by U.S. chemical manufacturers, as part of the process of selecting products and countries for this part of the study, we gathered some descriptive information on unregistered pesticides. For example, we used information presented in the Farm Chemicals Handbook to determine the intended use of these unregistered products (for instance, as a herbicide or fungicide) and the number of basic producers of each compound. (See table II.1.) According to this source, 1 of these products is manufactured by 12 companies and another by 13, 3 are manufactured by 2 companies, and 9 are manufactured by 1 company. In the following sections of this appendix, we present the remainder of the information we gathered, broken down by category.

Unregistered Pesticides With Pending Registrations

In a January 27, 1992, communication to the Senate Agriculture, Nutrition, and Forestry Committee, the National Agricultural Chemicals Association reported that 25 unregistered active ingredients were exported in 1990 and that, within this group, 11 ingredients had registrations pending with EPA. To verify this information and to obtain a sense of what "pending" status actually implies, we contacted the EPA product managers assigned to these products. For each product, we requested the date of the initial application for registration and the date that data were last submitted. We learned that one of these products is now registered and another has received a U.S. food tolerance, leaving eight products with pending registrations. The results of this effort are presented in table II.2.

Table II.2: Status of Pending Registrations

Active Ingredient	Date of initial application	Date of last data submission
Butachlor	6/29/78 (withdrawn) 12/23/91 (rice, import tolerance)	12/23/91
Carbendazim	12/7/87	3/8/90
Carbosulfan	9/30/82 (food use) 6/22/87 (nonfood use)	10/29/91
Ethametsulfuron methyl	10/91	10/91
Flusilazole	12/29/86	4/3/92
Haloxyfop (application for four different products)	7/30/85 4/11/89 9/20/89 5/15/91	3/13/92 2/12/92 11/02/90 1/02/92
Quinclorac	4/10/89	2/7/91
Tebucanazole	12/30/88	1/22/92

Source: Information provided by EPA product managers.

To summarize, table II.2 shows that the manufacturers of 5 products (carbendazim, ethametsulfuron methyl, flusilazole, quinclorac and tebucanazole) appear to be actively pursuing registration at this time, as evidenced by the recency of the initial registration application and the dates on which data were last submitted by the manufacturer. In addition, as table II.2 indicates, there are two compounds with registration applications that were initiated over 9 years ago. The manufacturers of these products initially sought food-use registrations; however, at present, they are either pursuing a nonfood-use registration (carbosulfan) or an import tolerance (butachlor).

Registration Status of Unregistered Pesticides in OECD Countries

We used the European Directory of Agrochemical Products computer data base, as well as published registration lists provided by OECD nations that responded to our survey, to determine where these products have been registered. We found that many of these pesticides have been widely registered by OECD nations. (See figure II.1.) This tabulation may slightly underestimate the number of OECD-country registrations that U.S.-manufactured unregistered pesticides hold. Confidential business information provided to us by chemical companies suggests that some of these products may have been granted registrations in other OECD countries. The public sources we used did not show such registrations.

Destination of Exported Unregistered Pesticides

We obtained export information on unregistered pesticides from foreign purchaser acknowledgement statements for 1990 submitted by pesticide manufacturers, which are required by FIFRA, section 17. This source indicated that unregistered pesticides are widely exported throughout the world, and that OECD nations import many of these products. (Data for this tabulation only included the unregistered pesticides listed in table II.1.) It should be noted that this information represents the best estimate of the final destination of these products. Transshipment is possible, however, since products exported to one country may be reexported to another nation. (See figures II.1 and II.2.)

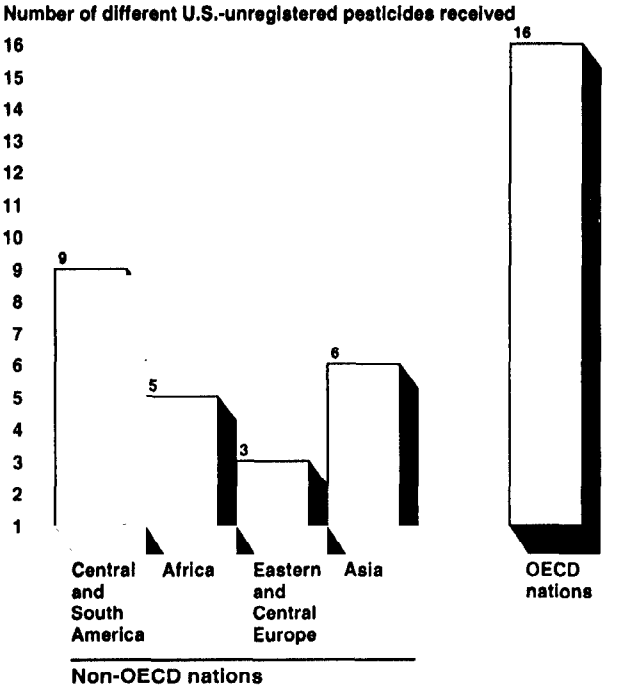
Figure II.1: Registrations Granted by OECD Countries for a Group of U.S.-Unregistered Pesticides[a]

U.S.-unregistered compounds	Countries where registered																				
	Spain	France	Belgium	Germany	New Zealand	Australia	Ireland	Italy	Switzerland	United Kingdom	Greece	Austria	Portugal	Luxembourg	Netherlands	Sweden	Canada	Denmark	Norway	Finland	Total
Carbendazim	x	x	x	x	x	x		x	x	x	x				x	x	x				13
Thiometon	x	x	x	x	x	x	x			x	x	x	x	x	x						13
Nuarimol	x	x	x	x			x	x	x	x	x		x	x				x			12
Alphamethrin	x	x		x			x	x		x		x	x		x	x		x			11
Carbosulfan	x	x	x	x			x	x		x	x					x					9
Flusilazole	x	x	x	x	x	x	x		x	x											9
Haloxyfop	x	x	x		x	x	x	x	x					x							9
Terbumeton	x	x		x	x			x			x	x	x								8
Tebuconazole	x		x		x				x										x		5
Ethametsulfuron methyl			x			x						x					x				4
Prosulfocarb	x	x		x					x												4
Cadusafos	x	x																			2
Prothiofos	x					x															2
Butachlor	x																				1
Esprocarb																					0
Ipsdienol																					0
Simetryn																					0
Total	13	10	8	8	6	6	6	6	6	6	5	4	4	3	3	3	2	2	1		

[a]Registration information was not available for Iceland, Japan, and Turkey.

Source: European Directory of Agrochemical Products and documents provided by OECD countries.

Figure II.2: Destinations of U.S.-Unregistered Pesticides, 1990[a]



[a]Destinations of U.S.-registered pesticides within OECD were Australia (6); France, Japan, and Switzerland (4 each); Germany (3); Belgium, Italy, New Zealand, and the United Kingdom (2 each); and Canada, the Netherlands, Norway, Spain, and Sweden (1 each).

Source: Foreign Purchaser Acknowledgement Statements, EPA.

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