“The need for generally accepted scientific principles and requirements in all areas of toxicology particularly applies to the newly developed field of neurotoxicology. Methods continue to be developed in isolation, and the comparability of results is often in doubt. Furthermore, until scientific principles have been agreed on, internationally accepted strategies to test the effects of chemicals on the many functions of the mammalian nervous system will not be developed.”

Principles and Methods for the Assessment of Neurotoxicity Associated With Exposure to Chemicals
World Health Organization, 1986

“The NACA supports additional neurotoxicological and behavioral effects testing as a legitimate component of the requirements for re-registration and registration.”

John F. McCarthy
Vice President for Scientific and Regulatory Affairs
National Agricultural Chemicals Association, 1989

“Exporting banned pesticides demonstrates that from the cradle to the grave—or from production to use and disposal—dangerous chemicals are discharged into our environment, and threaten the public health both here and abroad.”

Sandra Marquardt
Exporting Banned Pesticides: Fueling the Circle of Poison
Greenpeace USA, 1989
International Regulatory and Research Activities

This chapter examines the international regulatory and research programs devoted to neurotoxic substances in general and neurotoxic pesticides in particular. The first part of the chapter addresses the export of neurotoxic pesticides that have been banned or severely restricted (a limited ban) in the United States. Regulatory programs in foreign countries, both industrialized nations and developing nations, are discussed. The second part of the chapter focuses on international research activities. This chapter does not address the export of food additives, drugs, and other chemicals.

INTERNATIONAL REGULATORY ACTIVITIES

According to the U.S. General Accounting Office (GAO), from 1977 to 1987, the worldwide agricultural chemical market doubled in size, to more than $17 billion. U.S. pesticide export sales currently represent approximately one-quarter of the world pesticide market. Although U.S. export statistics vary, the best estimates conclude that about 400 to 600 million pounds of U.S.-manufactured pesticides are exported each year to foreign countries. According to GAO, unregistered pesticides, including banned or restricted pesticides as well as pesticides that may never have sought U.S. registration, now account for about 25 percent of all U.S. pesticide exports (61).

According to other estimates, the United States supplies approximately one-half of the pesticides imported in most Latin American countries, where a substantial amount of the fresh fruits and vegetables eaten in the United States in the winter months are grown (42). Figure 9-1 illustrates U.S. pesticide exports for 1983 to 1988. In recent years, approximately 50,000 different pesticide products have been registered for use by the Environmental Protection Agency (EPA) (61). This figure does not include pesticides that have never been registered but are manufactured and exported for use outside the United States. Figure 9-2 compares U.S. pesticide sales with world pesticide sales for 1987.

Some developing nations have few or no regulations to protect workers and consumers from the harmful effects of neurotoxic substances. Developing nations that do have regulations often do not have adequate resources to implement and enforce them. This lack of effective regulation and enforce-

Figure 9-1—Total U.S. Pesticide Exports, 1983-88

![Bar chart showing total U.S. pesticide exports from 1983 to 1988.](chart1)


Figure 9-2—U.S. and World Pesticide Sales (Basic Producer Level, 1987)

![Graph showing U.S. and world pesticide sales for 1987.](chart2)

ment in developing nations has a negative impact not only on the public health and environment in user countries, but also in industrialized nations, including the United States, where people process and consume imported crops that may contain pesticide residues.

Despite many regulations promulgated in this country for the protection of consumers and workers, U.S. citizens are exposed to banned and severely restricted pesticides through what has come to be referred to by critics as the ‘boomerang effect’ or the “circle of poison” (41,70). At times, food in U.S. supermarkets has been imported from developing countries where farmers use pesticides manufactured in the U.S. that have been banned, severely restricted, or never registered for use here. Figure 9-3 indicates the dollar value of total U.S. food imports from 1983 to 1988. One organization has estimated that 70 percent of the pesticides exported to developing countries are used on crops grown for export to industrialized countries (70). This effectively circumvents the protection that the regulatory action was intended to provide.

Federal law currently permits U.S. companies to manufacture and distribute banned, severely restricted, and never registered pesticides for use in developing nations, despite the possibility that food products containing residues of these pesticides may be imported to the United States and made available to U.S. consumers. Little definitive information exists on the identity and quantity of residues of banned, severely restricted, and never registered pesticides that return to the United States on imported crops and meats. This is due in part to the relatively small number of Food and Drug Administration (FDA) and U.S. Department of Agriculture (USDA) personnel available to screen sufficient quantities of imported crops and to limitations in the technology for detecting residues (62). However, data are available on the dollar value of crops that are produced domestically versus the value of crops that are imported. Figure 9-4 compares domestic production with imports of selected major crops. Some crops, such as coffee, are not produced domestically, so the United States must depend entirely on imports to supply consumer demand.

One example of the effect of current policies is the export of the insecticide chlordane. This product was taken off the U.S. agrichemical market in 1978 due to concerns about its carcinogenicity (it is also neurotoxic) and its persistence in animal fatty tissue and in the environment. Yet Federal law allows it to be manufactured and exported, without prior notification, to developing countries which do not have to adhere to U.S. use controls. Chlordane and heptachlor export formulations were both registered under section 3 of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) and as such are exempt from the export notification requirements imposed by language in section 17 of FIFRA. At least twice in 1988, adulterated beef from Honduras, contaminated with chlordane, was imported into the United States and consumed by people in Florida, Kentucky, and Minnesota before the contamination was discovered (33,54). In one such instance, the
chlordane residue was reported to be eight times the approved tolerance (33). Chlordane has been banned for all agricultural use in the United States yet is widely used in agricultural settings in countries such as Argentina, Australia, Colombia, and the Dominican Republic (33). In some cases, residues are not the result of direct application to crops or livestock. The Honduran problem was attributed to the use of chlordane on nearby sugarcane.

The misuse of registered chemicals, many of them neurotoxic, is an equally important issue (38). Registered chemicals used by untrained farmworkers without proper protective clothing and equipment, in inappropriate amounts on inappropriate crops, and without attention to other safety regulations, have been known to cause significant public health and environmental problems. Moreover, a substantial proportion of all pesticides are used to destroy pests that primarily affect the appearance of agricultural crops. Consumers often demand that their fruits and vegetables look “picture perfect”; however, cosmetic imperfections usually do not affect either the taste or the nutritional value of most foods (22). Although limited use of less hazardous pesticides is generally considered to be economically beneficial and to pose a minimal health risk, overuse of the more hazardous pesticides is an increasing concern among public health officials worldwide.

U.S. Regulation of Neurotoxic Substances

Export Laws

The United States has several laws governing export of toxic substances. The Toxic Substances Control Act (TSCA) was enacted in 1976 to address the risks presented by hazardous chemicals and is the primary statute regulating the export of industrial chemicals. Section 12 of TSCA addresses exportation of hazardous chemicals. Section 3017 of the Resource Conservation and Recovery Act (RCRA) discusses the export of hazardous waste, and section 17 of FIFRA governs importation and exportation of pesticides and devices.

Under TSCA, chemicals for domestic use that present an unreasonable risk of injury to humans and are imminent hazards to the environment can be regulated. The Act requires that regulation be done in such a way as not to impede unduly or create unnecessary economic barriers to technological innovation. Section 12 provides that, in most instances, the requirements of TSCA do not apply to substances manufactured, processed, or distributed for export. The requirements will apply, however, if it is determined that the substance, mixture, or article will present an unreasonable risk of injury to the health of persons within the United States or to the environment of the United States. The Act also provides that any person who exports or intends to export a substance for which submission of data is required under this Act must notify the Administra-
tor of the Environmental Protection Agency of the 
exportation or intent to export. Moreover, the 
Administrator shall then furnish to the government 
of the importing country notice of the availability of 
the data submitted for each substance.

RCRA provides for the management and disposal 
of solid wastes to avoid contamination of the 
environment. Section 3017 prohibits any exporting 
of hazardous waste unless the importing country has 
been given notice of and has consented to the 
shipment of the waste. However, exporters are not 
required to describe the contents or toxicity of the 
waste they are shipping. In addition, incinerator ash 
and municipal waste, both of which contain neuro-
toxic metals and chemicals, are not covered by the 
consent scheme.

Section 17 of FIFRA states that pesticides and 
devices intended solely for export are exempt from 
the testing and review requirements of the Act. 
Accordingly, pesticide manufacturers and dis-
tributors can legally export pesticides that have 
been banned or never registered for use in this 
country. Little is known about pesticides that have 
ever been registered because they are exempt from 
public health and environmental testing require-
ments if domestic use is not intended.

U.S. pesticide manufacturers are required to 
notify the importing purchaser, and EPA notifies 
the country, if the pesticide to be exported has been 
banned or never registered for use in the United 
States. EPA requires these statements annually for 
the first shipment of each banned or unregistered 
product to a particular purchaser for each importing 
country. Although EPA has streamlined the trans-
mittal process for export notices to U.S. embassies, 
no formal procedures govern the processing and 
transmittal of FIFRA notices once they arrive at an 
embassy. Most embassies destroy files as recent 
as 1985, and staff at every embassy surveyed by 
GAO indicated that they sometimes do not retain 
copies when transmitting files to the foreign govern-
ments. According to GAO, as recently as 1988, 
EPA had no program to determine whether 
pesticide manufacturers were complying with the 
export notification requirements and had no 
assurance that importing countries were ade-
quately notified of unregistered U.S. pesticides 
entering their borders. Moreover, shipment of 
the unregistered pesticide may proceed before the 
foreign government has received the notice, since its 
purpose is only informational.

Although the language in section 17(a) of FIFRA 
governing notification requirements for unregistered 
pesticides provides for no exceptions, EPA, in 1980, 
established a policy that effectively waives notifica-
tion requirements for unregistered pesticides that are 
“minor variations” on formulations and active 
ingredients registered in the United States and that 
are “similar in composition and use” to registered 
pesticides. These exempted pesticides are com-
monly referred to as “me-toos.” Thus, never-
registered pesticides must bear the statement “Not 
Registered for Use in the United States of America” 
when they are exported to foreign markets, but 
me-toos are exempt from the labeling requirement, 
despite the fact that the active ingredient and inert 
ingredient formulation may be different from that 
registered in the United States and thus pose a 
different risk. Accordingly, it would be difficult 
for an importing foreign purchaser or nation to know 
the degree of hazard of such a product. Moreover, 
GAO determined that EPA did not send required 
notices for three of four pesticides, despite the fact 
that they were voluntarily canceled because of 
concern about toxic effects. Although EPA 
finalized cancellations of these four pesticides 
between 1975 and 1987, a notice was issued on only 
one of them. Consequently, foreign govern-
ments may not be alerted to unreasonable hazards 
associated with using particular pesticides.

Section 17(b) of FIFRA requires that EPA notify 
foreign governments and appropriate international 
agencies “[whenever a registration, or a cancella-
tion or suspension of the registration of a pesticide 
becomes effective, or ceases to be effective. . . .” 
EPA has no regulation or formal policy statement on 
when to issue such a notice. Instead, the Agency 
issues notices for cancellations and suspensions it 
deems to be of “national or international signifi-
cance.” EPA periodically publishes a booklet 
summarizing and clarifying its actions on canceled, 
suspended, and restricted pesticides; however, 
this booklet was last published in 1985. If updated 
anually, this booklet could be used by foreign 
governments and others as a reference guide to U.S. 
regulatory actions on pesticides.

On January 15, 1981, several days before the end 
of his term, President Jimmy Carter issued Execu-
tive Order No. 12264, “On Federal Policy Regard-
ing the Export of Banned or Significantly Restricted Substances,” including pesticides. This order put controls on exports of substances that were banned or severely restricted in the United States. Several days after becoming President, Ronald Reagan revoked the order.

Regulation of Pesticide Residues in Domestic and Imported Food

Federal jurisdiction over pesticide residues in food is divided among three agencies—EPA, FDA, and USDA. Their authority derives primarily from five laws: FIFRA; Federal Food, Drug, and Cosmetic Act (FFDCA); Federal Meat Inspection Act (FMIA); Poultry Products Inspection Act (PPIA); and Egg Products Inspection Act (EPIA) (62).

Under FIFRA, a pesticide must be registered (even conditionally) or have its registration pending before it can be used in the United States. In registering a pesticide, EPA considers the results of numerous public health and environmental fate studies (submitted by the manufacturer) to determine the risks and benefits associated with the use of that pesticide. Registration includes identification of the specific commodities on which the pesticide can be used. During the registration process, EPA attempts to determine if the pesticide’s use will cause an unreasonable risk to humans or the environment (see ch. 7). The registration requirements for pesticides are set forth in section 3 of FIFRA and are defined more fully in EPA regulations (40 CFR 1987 ed. 158, 162).

If use of a pesticide will leave a residue on food or feed commodities, EPA, under FFDCA, establishes a legal maximum level, or “tolerance,” for the pesticide residue. A tolerance, or an exemption from a tolerance, must be granted before a pesticide is registered. Tolerances cannot be legally exceeded, and residues of pesticides for which no tolerance has been established or exempted are prohibited on foods. Commodities that violate these prohibitions are subject to seizure by FDA, USDA, or a State enforcement agency (62).

If a pesticide has never been registered for use in the United States and the manufacturer does not expect residues to occur on imported foods, a tolerance will not necessarily have been set. Also, tolerances may not have been established if a registration application is pending. Any imported food contaminated with a pesticide that does not have a tolerance is considered adulterated and is subject to seizure at the U.S. border. However, if USDA and FDA border inspectors are not told that these pesticides have been used or they are unable to test for them, illegal residues in imported food will not necessarily be detected.

One pesticide industry spokesman has indicated that increased monitoring for pesticide residues would strengthen and bolster U.S. consumer confidence in the quality of the food supply (35). Additional testing of agricultural chemicals, called “reregistration,” is under way, and over the next 9 years, the agricultural chemical industry expects to pay $170 million in fees to help EPA finance the effort (35).

FDA, under FFDCA, is responsible for enforcing tolerances established by EPA for food and animal feed in interstate commerce. It is also responsible for enforcing the prohibition in food or animal feed of residues of pesticides for which no tolerance has been set or exemption given. In the past, when FDA considered low levels of a residue to pose little risk to human health, it would set informal residue levels, called action levels. At these levels, FDA would take regulatory action; below them the food was considered safe. A recent court opinion struck down
this practice, and EPA and FDA are currently determining how to address this issue.1

The USDA is responsible for enforcing tolerances in meat and poultry under authority of the Federal Meat Inspection Act and the Poultry Products Inspection Act. It is also responsible for monitoring pesticide residues in raw egg products (dried, frozen, or liquid eggs) and for enforcing tolerances at establishments having official USDA egg products inspection services, under authority of the Egg Products Inspection Act (62). While most of the focus has been on food crops, more insecticide is used on cotton on a worldwide basis than any other crop (23).

**International Effects of U.S. Export Practices**

Regulations governing the export and import of neurotoxic substances are far from uniform. Many nations, including the United States, have policies and procedures in place, but too often they work only on paper. In practice, they may allow neurotoxic substances to slip through the regulatory cracks. Regulatory requirements designed to protect workers and consumers from the harmful effects of toxic substances may be ineffective in some countries. The United Nations Food and Agriculture Organization (FAO) has implemented an International Code of Conduct on the Distribution and Use of Pesticides to outline responsible behavior on the part of persons who deal with pesticides. Pesticides are known as the group of chemical products that includes insecticides, acaricides, molluscicides, rodenticides, nematicides, anthelmintics, fungicides, and herbicides (26). Although many consider the code a step in the right direction in terms of providing notification, use, and transport protections (among others), it is only a voluntary code, and FAO has no enforcement authority. The objectives of the code are to set forth standards of conduct for all entities engaged in distributing and using pesticides. Pesticides are biologically active, and their uncontrolled release will always present a potential threat to the environment (27). The code describes the shared responsibility of many segments of society, government, industry, trade, and international institutions to use pesticides when necessary without adversely affecting people or the environment (40).

The Pesticide Development and Safe Use Unit of the International Program on Chemical Safety has toxicologically evaluated 83 pesticides widely used in agriculture and public health and established average daily intake and maximum residue limits for 23 of them (43). The Codex Alimentarius Commission (Codex) has established maximum residue tolerances for numerous chemical residues, contaminants, and food additives (43). Sampling and analysis principles to determine pesticide residues in food and animal feed have also been developed (43).

Despite numerous regulations governing the export and import of pesticides and other neurotoxic products in the United States and abroad, some countries do not have the regulatory framework and resources to adequately protect human health and the environment from these substances. Nearly all major U.S. corporations producing pesticides that have been banned, severely restricted, or never registered for use in the United States are multinational and have subsidiaries or other distributors in developing countries. In some cases it is through these subsidiaries and distributors that such pesticides are imported and distributed in developing countries. This also allows corporations with stocks of toxic substances that can no longer be sold in the United States to sell existing products.

In addition to concern about food products that are imported into the United States with residues of banned, severely restricted, or unregistered pesticides, critics are concerned that exported pesticides may not be properly packaged or labeled. At times, the package labeling and instructions may be written in English instead of the native language of the importing country. In some cases, farmworkers using the pesticides are illiterate and thus could not read the labels even if they were written in their native language.

Improper labeling may prevent implementation of appropriate safety measures or precautions by farmworkers and consumers. In July 1986, phosdrin, a potent neurotoxic insecticide classified by the World Health Organization (WHO) as “extremely hazardous,” was purchased in Benguet Province, Philippines. The product label had seven labeling infringements, all of them in direct violation of the FAO code (20). Similar violations of the FAO code have

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1Sec. 21 CFR secs. 109 and 509, 1987; FDA Compliance Policy Guides, 1986. The informal process by which these action levels were set was vacated by the Federal Appeals Court in the District of Columbia Consumer Nutrition institute v. Young, 818 F.2d 943 (D.C. Cir. 1987).
been discovered recently in Ecuador, Papua New Guinea, Thailand, Senegal, Colombia, South Korea, Sudan, and Mexico (18). In Iraq in 1973, an epidemic of methyl mercury poisoning resulted from improper labeling. Farmers and their families ate bread made from seed treated with mercury. The bags in which the grain was imported were clearly labeled in English and Spanish (neither of which is a native language of Iraq). More than 1,000 people died from mercury poisoning, and 10 times more were hospitalized (see box 2-A, in ch. 2) (2).

In some instances, even if the pesticide is properly packaged and labeled when it leaves the exporting country, it is repackaged in the importing country without the necessary labeling. Accordingly, the pesticide product that actually reaches the user may lack very important health and safety information. Repackaging is frequent, because pesticides are often shipped in 35- to 100-gallon drums and are then transferred into smaller, more manageable sizes for the consumer. On an international scale, pesticides are widely available to the general public, and few warnings are given (18). In some countries, pesticides are sold in markets alongside vegetables and grains. People can scoop up pesticides in cartons, bottles, cans, plastic or paper bags—whatever they bring to the market. Often they do not know the name of the chemical they are purchasing because the container is not labeled. In some countries, pesticides are marketed as “plant medicines,” and farmers are encouraged to use them to keep their crops healthy in much the same way that medicines are used to keep people healthy (24).

The pesticide industry is aware of the illiteracy problem and is taking steps to circumvent it. One approach is to use illustrations, or “pictograms,” that convey to an illiterate worker the appropriate way to mix, use, store, or clean up pesticides. These pictograms were designed by the International Group of National Associations of Manufacturers of Agrochemical Products, an international consortium of pesticide manufacturers, formulators, and distributors, in cooperation with the FAO. Figure 9-5 shows examples of pictograms currently used by some pesticide companies in developing countries. It is not yet known how extensively the pictograms are used or with what degree of success.

It is not only in export and use that pesticides pose problems, however. Pesticides are frequently manufactured in developing countries, where there are less stringent regulations. U.S. manufacturers claim that it is safer to produce pesticides in the United States, with its many regulations, than in developing countries. The combination of lethal ingredients and deficient safety precautions was dramatically demonstrated by the 1984 leak at the Union Carbide pesticide plant in Bhopal, India, which killed more than 2,000 people and injured tens of thousands (69).

Pesticide manufacturers justify U.S. export practices and advocate increased use of pesticides by maintaining that developing nations need pesticides to combat famine. The world population is growing rapidly: in 1975 it was 4.1 billion; in 1987 it had grown to 5.1 billion; and the projected figure for 2005 is 6.7 billion (64). Feeding this ever-increasing population is a problem because land available for farming is not increasing significantly. Moreover, the population increase is greatest in developing nations.

Critics of U.S. export practices argue that pesticides in the developing world are more often applied to luxury export crops than to staples eaten by local inhabitants and that, in any case, nonchemical methods of pest control could and should be implemented (70). According to the World Bank, the world produces enough grain alone to provide every human being on the planet with 3,600 calories a day (72). In a major 1986 study of world hunger, it found that a rapid increase in food production does not necessarily result in less hunger. Hunger can only be alleviated by redistributing purchasing power and resources to those who are undernourished (72). In India, for example, despite a 24-million-ton grain surplus (25), per-capita consumption of grain has not increased in 20 years and nearly half the population lacks the income necessary to buy a nutritious diet (63). Availability of grain in India has actually declined in recent years, despite a rise in pesticide use (57). Furthermore, numerous plantations and other agricultural areas have been forced to turn away from pesticide use due to resistance problems developed by insects, weeds, and fungi overdosed with pesticides (23).

The USDA has addressed the issue of world hunger, particularly in developing nations, as follows:

First, the food problem of the developing countries is not a global lack of food. More than enough food is produced and stored in the world to provide...
Figure 9-5-Pictograms for Agrochemical Pesticides

Storage pictogram
- Keep locked away and out of reach of children

Activity pictograms
- Handling liquid concentrate
- Handling dry Concentrate
- Application

Advice pictograms
- Wear gloves
- Wear eye protection
- Wash after use
- Wear boots
- Wear protection over nose and mouth
- Wear respirator

Warning pictograms
- Dangerous/harmful to animals
- Dangerous/harmful to fish—do not contaminate lakes, rivers, ponds, or streams

people everywhere with adequate diets. In times of crises, countries have the capacity to respond quickly with food and other needed supplies to alleviate hunger and suffering. Unfortunately, political differences within and between countries and logistics sometimes impede the efforts to save lives, as in the current food crisis in sub-Saharan Africa (59).

Regulatory Policies in Other Industrialized Nations

For the most part, regulations in industrialized countries are enforced, and public health and environmental problems from pesticide importation, distribution, and use are not as severe as in developing nations. However, this does not mean that pesticide problems are nonexistent in industrialized nations. The following discussion summarizes the activities of some industrialized nations with major regulatory programs.

Canada

Within Canada primary responsibility for environmental issues with international and interprovincial components lies with the federal government, while the provinces are generally responsible for enforcing regulations governing industries within their borders (12). Environment Canada, established in 1971, is the federal department that administers legislation relating to environmental protection. A major reorganization of Environment Canada in 1986 and 1987 consolidated the department’s activities into three main branches: Conservation and Protection, Atmospheric Environment (responsible for meteorology), and Parks (responsible for maintenance of national parks). Conservation and Protection includes the Canadian Wildlife Service, Environmental Protection, and the Inland Waters and Lands Directorate.

The primary federal legislation controlling the availability, sale, and use of pesticides is the Pest Control Products Act, administered by Agriculture Canada (12). The Act requires annual registration of pesticides and prohibits import or sale of unregistered pesticides. It is intended to ensure that no person shall use a pesticide under conditions that are unsafe to human or animal health or that will adversely affect the environment. The Act also requires that such products be effective for their intended purposes (46). There are currently plans to upgrade the legislation to require more stringent testing of pesticide products.

Agriculture Canada calls on various federal departments to provide expert advice on hazards that may be associated with the use of a product. Health and Welfare Canada requires and reviews a range of toxicological studies to assess potential health hazards that may be associated with exposure to a chemical, including acute, subacute, chronic, reproduction, teratology, and metabolism studies. In addition, studies to estimate anticipated human exposure during typical field use of the chemical are required.

The federal departments primarily involved in the pesticide review process are Agriculture Canada, Fisheries and Oceans Canada, Environment Canada, and Health and Welfare Canada (12). The Pesticides Directorate of Agriculture Canada receives the manufacturer’s application for registration of the pesticide and is responsible for the evaluation process and the coordination of reviews from the other agencies (46).

Federal Republic of Germany

The Federal Republic of Germany, one of the world’s largest exporters of pesticides, divides and sometimes shares lawmaking and enforcement powers between the federal government (Bund) and the 11 states (Lander). The Federal Ministry for Environment, Nature Protection, and Nuclear Safety was created in 1986, in the aftermath of the accident at the nuclear power plant in Chernobyl in the Soviet Union. It was created out of the Environment and Nuclear Safety divisions of the Ministry of Interior and the Nature Protection Division of the Ministry of Nutrition, Agriculture, and Forest (MNAF) (14).

Pesticides are regulated under the Pfalnzen- schutgesetz (Plant Protection Law), which outlines the terms of licensing, prohibition, or restriction of use, application, and export (43). Licensing, which is issued only if the pesticide is safe, efficacious, and in compliance with requirements for human and animal health and safety, provides for classification, testing, labeling, and packaging (43).

The Federal Environmental Agency (FEA), under the authority of the MNAF, is responsible for general environmental policy-related research, including maintenance of an environmental information planning system, collection of information necessary to develop and implement federal laws, and preparation of legislation and administrative regulations. The FEA has done considerable work
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on the development of environmental impact assessment procedures (14). A separate organization, the Conference of State Ministers for the Environment, which includes the Federal Environment Ministry, is the major forum for coordination of state and federal environmental policy. Federal-state working committees have been established to coordinate programs in all major areas of environmental protection (14).

The Federal Ministry for Foreign Affairs is responsible for international relations and environmental policy. The Federal Ministry of Food, Agriculture, and Forestry houses the Agricultural Research Center, which monitors soil biology, agrichemicals, agricultural waste recycling, plant ecophysiology, and water pollution, and the Federal Center for Biological Research in Agriculture and Forestry, which is responsible for pesticide measurement and control, biological pest control, and inspection of commercial chemical preparations for plant protection and pest control (14).

A number of environmental laws are in effect. The Act on Protection Against Dangerous Substances, which was adopted in 1980 and amended in 1986, establishes a testing and notification system for new chemical substances placed on the market after September 1981. The Act seeks to protect public health and the environment from harmful effects of dangerous substances by: 1) compulsory testing of and notification regarding substances; 2) compulsory classification, labeling, and packaging of dangerous substances and preparations; 3) prohibitions and restrictions on use; and 4) specific legal provisions concerning toxicity and occupational safety. The Act covers foodstuffs, tobacco products, cosmetic agents, animal feedstuffs and additives, pharmaceuticals, wastes, radioactive wastes, waste water, and waste oils (14).

The Act requires notification at least 45 days prior to placing a substance into initial circulation in a country that is a member of the European Community (EC), whether on a commercial basis or within the framework of any other business undertaking. There is no requirement for notification if the substance was manufactured and notified by an equivalent procedure in any other EC member country (14). Six administrative regulations have been adopted concerning information required in notifications, designation of the Federal Office for occupational and Safety Policy to receive notification, inventory of existing chemical substances, labeling of hazardous substances, and general administrative procedures.

Criminal violations of environmental legislation are generally codified in division 28 of the criminal code, adopted in 1975 and last amended in 1987. Penalties range from fines to jail sentences and are usually defined in the particular environmental law (14).

Belgium

Environmental programs in Belgium are less well developed than those in other European countries. Because implementing legislation must, in most instances, be enacted by the regional administrations, norms and enforcement vary throughout the country (11).

A 1969 act regulates the manufacture, composition, storage, transport, and marketing of pesticides. Such activities may be carried out only by licensed persons. The maximum concentrations of residue after decomposition may also be controlled under the act, as well as the conditions of use of pesticides. Pesticides themselves are subject to an approval procedure, and the license usually lasts for 10 years. The approval is made subject to conditions, and it is an offense to use pesticides other than in accordance with these conditions (11).

A royal order of 1975 regulates the storage, trade, and use of pesticides and plant protection products. Pesticides are subject to premarket registration, and certain labeling and packaging requirements are set out (11). A royal decree of 1977 implements EC Directive 76/1 16, which prohibits the marketing of manure and fertilizer, as well as all products with a specific action to stimulate crop production. This decree also regulates the information and indications to be put on the package, the documents required for transport, the packaging requirements, and the method of taking and analyzing samples (11).

A royal decree of 1982 requires that before placing a dangerous substance on the market, any manufacturer or importer must submit to the Minister of Public Health a dossier that includes a declaration of the unfavorable effects of the substance for the various uses envisaged. The decree establishes a Committee on Dangerous Substances, composed of officials of different ministerial departments and attached to the Ministry of Public Health. The committee is responsible for examining the
notification procedure and advises on the completeness of the application. A dangerous substance cannot be placed on the market during the 45 days it takes to complete the notification procedure (11).

France

Pesticides for agricultural use are governed by a 1972 law that controls manufacture, sale, and use as well as packaging and labeling (43). Prior to approval for production, toxicity and efficacy must be assessed, and the pesticide must be classified in terms of toxicity (43). Tolerance limits in foods are prescribed by presidential decree (43).

The Chemicals Control Law, adopted in 1977, governs hazardous substances. It is intended to protect public health and the environment against risks that may arise from natural or industrially produced chemicals, but it does not apply to chemicals used in research or to food additives, cosmetics, or drugs (13). The law provides for premanufacture notification for all chemicals that have not yet been marketed. Producers or importers must declare any new risk that may result from a change of manufacturing process or from emission of the said chemical into the environment (37).

Producers or importers of new chemicals must also submit a technical dossier providing the information needed for assessment of potential hazards. The competent authority may classify a substance as a “dangerous product” request from the manufacturer or importer any relevant information with respect to potential health or environmental effects; and prohibit or restrict the production, composition, storage, transportation, conditioning, labeling, marketing, use, or disposal of any chemical where deemed necessary to protect the public (37).

Producers of already marketed substances maybe required to provide public authorities with appropriate technical or toxicological data to evaluate potential health or environmental risks. Violation of the law may result in imprisonment or fines or both.

Japan

Agricultural chemicals are regulated by a 1948 law that has been amended several times, most recently in 1983 (43). It requires that pesticides be registered with appropriate government agencies, which classify pesticides according to persistence in crops and soil and water pollution potential (43). Limits are placed on the amount of active ingredients and the maximum allowable harmful ingredients for each pesticide (43). The applicant must provide test results on pesticide effectiveness, toxicity, phytotoxicity, and persistence (43). Labeling and packaging must represent truthfully all statements and facts on which the pesticide was registered and must include, among other things, the dangers posed and precautions to be taken for storage and use (43).

Other toxic substances are regulated by the Chemical Substances Control Law of 1973. The need for comprehensive measures to prevent environmental pollution has been recognized following environmental crises such as the mercury poisoning incident at Minamata Bay in the 1950s (see ch. 2).

The law requires notification and testing of all new chemical substances produced in quantities exceeding 100 kilograms. The law does not apply to chemicals in use before the law came into effect, but an agreement reached in the Diet makes some 800 existing chemicals subject to the same review standards as the new substances. The law also provides that, prior to production or importation, all new chemicals must be submitted to official examination regarding persistence, accumulative tendency, and toxicity to human beings.

A substance may be classified as a “specified chemical substance” if it accumulates easily in biological organisms, if it resists chemical changes caused by natural effects, and if it may harm human health when ingested over a period of time. The law was passed in response to polychlorinated biphenyl (PCB) poisoning (9). Chemicals tested and designated “specific substances” are subject to prohibition or restriction. Although only PCBs have been formally listed as specific substances under the law, government officials say that two or three chemicals are withdrawn from testing every month when manufacturers learn that the chemicals probably would be specified and the manufacturer’s name revealed. Another two or three applications for approval are suspended each month for lack of data (9).

The Pollution-Related Health Damage Compensation Law of 1974 was further modified, in the case of Minamata victims, by the Minamata Relief Law in 1978. The beneficiaries of this law are the victims of certain pollution-related diseases who have ‘lived, worked, or otherwise been present” in designated areas. Testing for functional developmental disor-
ders, including behavior disorders, has become one of the most important aspects of the evaluation of developmental toxicity of chemicals, especially pharmaceutical drugs. There are two guidelines for developmental toxicity testing of chemicals—one a three-segment study for drugs, the other a multigeneration study plus embryotoxicity for environmental chemicals (56). In the case of specific diseases, where the source of pollution is known, the company responsible must pay compensation. In nonspecific cases, there is a levy on polluting industries to cover claims. Certified victims, that is, persons who have been examined by government medical panels, are entitled to medical care expenses and a monthly physical handicap payment, the amount being determined by the victim’s age, sex, and ability to work. There are also child compensation allowances and survivors’ benefits. Payment is made by local governments through the Pollution-Related Health Damage Compensation Association. The government covers the association’s overhead costs, but payments to victims are financed by polluters.

United Kingdom

Pesticides are regulated under the Dangerous Substances Regulations and the Food and Environment Protection Act (43). The regulations specify which toxicity tests are necessary to categorize each pesticide, based on EC Directive 78/631 of 1978 (43). Packaging and labeling requirements are also set out in the regulations (43). Pesticide manufacturers must notify the government prior to marketing a new pesticide or suggesting new uses of an old one (43). Manufacturers must also provide sufficient data to enable government assessment of pesticide dangers, and warnings, precautions, and names of active ingredients must be included on all labels (43). The government has authority to request withdrawal of unsafe products and to specify maximum pesticide residues on crops, foods, and livestock feed (43).

Regulatory Issues in Developing Nations

In 1987, a new, centralized agency was formed to enforce environmental laws and regulations in England and Wales. Her Majesty’s Inspectorate of Pollution brought together several existing pollution control agencies: HM Industrial Air Pollution Inspectorate, for controlling major emissions to the atmosphere; HM Radiochemical Inspectorate, for controlling all radioactive discharges and disposals; the Hazardous Wastes Inspectorate, for monitoring the activities of local Waste Disposal Authorities; and the divisions of the Department of the Environment and the Welsh Office responsible for issuing consents for discharges by the Water Authorities.

Regulatory Issues in Developing Nations

Developing nations, especially those with a large agricultural economy, depend on pesticides to produce maximum yields. In many of these nations, agriculture is the primary industry and provides the country’s primary income. In Ghana, for example, cocoa exports provide a majority of foreign exchange earnings (8). Misuse and excessive use of pesticides and chemicals are a significant and widespread problem in developing countries (15). The WHO has estimated that someone in a developing country is poisoned by pesticides...
every minute (65). This is due in part to lack of a pesticide policy in many developing nations. The FAO estimated in 1988 that some 50 countries still did not have pesticide regulations (20). Those nations with a policy often do not have the infrastructure or economic resources to implement the policy. Moreover, in some developing nations, government officials charged with enforcing pesticide policies have a vested financial interest in maintaining a strong pesticide economy (20). In fact, the governments of many countries are pesticide importers, manufacturers, and exporters, as well as regulators of pesticides (20). Consequently, regulations designed to protect public health and the environment may receive little attention. In other cases, pesticides are heavily subsidized, making it cheaper to use pesticides than not (45).

Because of the lack of governmental controls, many developing nations must depend on the pesticide industry to regulate the importation, distribution, and use of pesticides, as well as to safeguard public health and the environment. In light of this, discussions of regulatory policy often focus on how much responsibility pesticide manufacturers and the governments of pesticide exporting countries should assume. Nations around the world agree that responsibility for safety and efficiency in distribution and use of pesticides must be shared by foreign manufacturers, exporters, and importers, as well as local formulators, distributors, repackers, advisers, and users (58). To facilitate the implementation of this duty, FAO adopted in 1985, and amended in 1987, a code covering such issues as proper pesticide transport, marketing and advertising, recalls, and notification on the part of regulators and manufacturers.

The code calls on industry to adhere voluntarily to its provisions and places an even higher responsibility on industry in countries that lack appropriate pesticide legislation and advisory services (58). The code maintains that manufacturers have a duty to retain an active interest in following their products to the ultimate consumer. Some assert that the ultimate consumer is the local farmer who buys a small amount of repackaged pesticide product for use. Following this line of reasoning, the manufacturer’s duty would end with this purchase. On the other hand, there is the argument that a farmer who produces cash crops, as distinguished from a subsistence farmer, is not a consumer but a producer (6). These producer-farmers use factors of production—land, seed, labor, water, fertilizer, pesticides—to produce a cash crop. The consumerism the person who buys the produce with the intent of eating it. Accordingly, the pesticide manufacturers have a duty to retain an active interest in following their products—pesticides—to the dinner tables of the families and individuals of the world community(6). One could further argue that U.S. manufacturers have a special duty to protect and ensure the safety of food treated with U.S.-manufactured pesticides and eaten by U.S. consumers, regardless of where that food is grown.

One controversial provision of the code intended to address the issues of regulation and education is that of prior informed consent (PIC). Under PIC, a pesticide that has been banned or severely restricted in one country cannot be exported to another country unless the importing country’s government has been fully informed of the reasons for the regulatory action and has consented to the importation of the pesticide (58). Pesticide exporting countries generally do not favor PIC and assert that it is too time-consuming, expensive, and burdensome for industry (20). Representatives of importing countries, on the other hand, claim that, in the absence of regulatory controls, PIC is the only avenue for allowing governments to determine if pesticides banned in other countries should be permitted within their borders. Although PIC is still a voluntary practice, the Netherlands became the first country to incorporate it into legislation and seek to make it legally binding (20).

The WHO has classified pesticides on the basis of the hazards they pose. Hazard is defined as the likelihood that a pesticide will cause immediate or short-term adverse effects or injury under circumstances of ordinary use. These classifications are based on the oral and dermal toxicity of the pesticide’s active ingredient. Countries adopting the FAO code are also supposed to adhere to the following WHO toxicity classification in labeling their pesticides:

- IA Extremely Hazardous,
- IB Highly Hazardous,
- II Moderately Hazardous, and
- III Slightly Hazardous.

In addition, the Pesticide Action Network (PAN) has initiated a Dirty Dozen Campaign on an international scale to publicize the 12 most hazardous pesticides used worldwide, most of which are
neurotoxic. Since the campaign began, some countries have banned certain pesticides on the Dirty Dozen list, and others have restricted the availability of them (20). The pesticides are:

- camphechlor (toxaphene),
- chlordane/heptachlor,
- chlordimeform (Galecron),
- dibromochloropropane (DBCP),
- DDT,
- aldrin/dieldrin/endrin,
- ethlene dibromide (EDB),
- lindane/hexachlorocyclohexane (HCH),
- paraquat,
- ethyl parathion,
- pentachlorophenol (PCP), and
- 2,4,5-T.

Pesticide workers in developing countries are frequently not provided with appropriate protective clothing and equipment to guard against oral and dermal exposure when applying pesticide products (30). In tropical or semitropical climates, the temperature is often too hot to permit workers to comfortably wear protective clothing designed for use in more temperate climates (protective clothing is often made of plastic, rubber, or other nonporous material). Despite workers’ lack of protective clothing, pesticides are sometimes sprayed from aircraft while workers are in the fields. Pesticides may also be sprayed from canisters strapped to the backs of unprotected workers.

Besides allowing the export of pesticides that have been banned or severely restricted for use in this country, present EPA regulations allow the export of pesticides that have never been reviewed by the Agency. Some critics argue that if a pesticide is not safe enough for use in the United States, it should not be exported. The FAO code holds that the fact that a product is not used or registered in the exporting country is not necessarily a valid reason for prohibiting export of that pesticide (58). Most developing countries are located in tropical and semitropical regions. Their climatic, ecological, agronomic, and environmental conditions, as well as their social and economic needs, may be different from those of industrialized nations. Accordingly, their pest problems may be quite different. The government of the exporting country, therefore, may not be in the best position to judge the suitability, efficacy, safety, or fate of the pesticide under conditions in the country where it may ultimately be used.

Critics of this export policy argue, however, that foreign relations problems could arise if products considered too unsafe and hazardous for use by people in the United States are deemed safe for use by people abroad. Although people in developing countries use only 10 to 25 percent of the world's pesticides (7,21), it is estimated that they account for as much as 50 percent of the acute poisonings of pesticide applicators and between 73 and 99 percent of their deaths (15). Furthermore, residents of the exporting nation are exposed to potentially dangerous chemicals during domestic production and eventual consumption of imported foods treated with the pesticides.

Following is a summary of regulatory activities in certain developing countries where pesticides are used. Boxes 9-A and 9-B illustrate problems that have occurred in developing nations. Although each of the profiled countries has some regulatory structure in place, each also has many problems with the import, distribution, and use of pesticides, resulting in health problems of varying degrees for farmworkers and consumers. In selecting the countries for this section, an attempt was made to obtain a geographic spread.

Malaysia

The Pesticides Board under the Malaysian Department of Agriculture has regulatory authority for pesticides in Malaysia. The Pesticides Act, the Pesticide Registration Rules of 1976, the Pesticide Rules on Importation for Educational or Research Purposes of 1981, and the Food Act of 1983 set out the language governing pesticide use (39).

Malaysia follows FAO guidelines with respect to data requirements for pesticide registration. However, all data, including efficacy data, may be from foreign sources. Data are evaluated and a recommendation is submitted to the Pesticides Board, which has authority to grant registration (39). Accordingly, a pesticide may be reviewed and approved for use in Malaysia with the approving authority depending entirely on data from the country of export.

The Department of Customs controls the import of all pesticides except those imported for research purposes, which are controlled by the Malaysian Department of Agriculture. The Department of Agriculture also controls the production, sale, and
Box 9-A—Problems With Neurotoxic Pesticides in Developing Countries

Irregularities concerning labeling, packaging, storage, sale, import, and advertising of pesticides have caused illness, injury, and death in many developing countries, as the following examples illustrate:

Pesticides are commonly repackaged without labels in Senegal, but labels are of little use anyway, because most pesticide users are illiterate. Instructions such as “in case of intoxication, call a doctor” are meaningless in rural areas where there are no doctors for miles, no telephones, and only sporadic transport.

In Indonesia, an outbreak of mosquito-spread dengue fever caused several deaths. The Ministry of Health sent an officer to spray the area with malathion, a class HI, slightly hazardous pesticide. The officer was photographed spraying malathion while children were running behind him to play in the pesticide mist (see photograph above).

In Papua, New Guinea, very few companies provide labels in Tok-Pisin, the widely spoken local language. Some pesticide products had labels in French. One pesticide, selecron, was found in stores with no label at all.

Many of the pesticides in Thailand, Indonesia, and the Philippines do not have child-proof packaging. Some liquid pesticides have easily opened screw caps, and powdered pesticides can be bought in plastic bags that an older child can open.

In Indonesia, some pesticides were repackaged into clear plastic bags without labels. Workers wore no masks or gloves. Unlabeled bags of temik, which is 10 percent aldicarb, a class IA, extremely hazardous neurotoxic pesticide, were available in stores. Aldicarb is more acutely toxic to mammals than any other pesticide presently in use.

In the Sudan, a family of eight died in 1985 from eating pesticide-poisoned bread made from pretreated wheat meant for seed. The pretreated wheat had been in badly labeled sacks stacked next to consumable wheat in an agricultural store.

In Brazil, a 1987 advertisement described deltamethrin as “the safest insecticide in the world.” Deltamethrin is classified as class II—moderately hazardous by the International Code of Conduct on the Distribution and Use of Pesticides of the Food and Agriculture Organization of the United Nations.

In Senegal, used pesticide containers are often recycle-d to carry food, milk, or cooking oil. In one village, 19 people from two families died as a result. The cook used oil sold in a bottle that had previously contained ethyl parathion, a class Ia, extremely hazardous pesticide.

In Brazil, when a number of states passed laws banning imports of pesticides banned in their countries of origin, translational pesticide corporations and importers filed legal action and succeeded in getting the laws declared unconstitutional.


use of pesticides and checks for compliance with regulatory policies. The Pesticides Board regulates advertisements of pesticides (39).

Residues on vegetables are monitored under the Food Act of 1983. To date, there is no system for monitoring pesticide poisoning except for occasional reports from hospitals. Following the deaths of two teenage girls from field exposure to paraquat in 1985, it was revealed that 1,200 workers had been killed by exposure to just that one pesticide (48). Both government and the private sector have implemented training programs on the safe handling of pesticides. These programs are geared toward farmers, applicators, dealers, distributors, manufacturers, and medical personnel (39).

Residues on vegetables are monitored under the Food Act of 1983, which prescribes maximum residue limits (5). In reality, monitoring and testing
Box 9-B—Incident at Lake Volta, Ghana

In Achedemade Bator, a fishing village on Lake Volta, a serious poisoning incident resulted from improper use of Gammalin 20, the trade name for lindane, a potent neurotoxic substance. The villagers, almost all of them illiterate, derived their income through fishing on the lake. The village fishermen discovered that by pouring lindane into the lake, fish would float to the surface and could be easily caught. This proved to be a very quick and efficient way of hauling in a catch. Any fish not consumed were salted, smoked, or sold.

Exposure to lindane may cause dizziness, headaches, convulsions, muscle spasms, brain disturbances, and unconsciousness. Some villagers experienced symptoms of lindane poisoning from consuming poisoned fish and using the lake as a source of drinking water but never associated their health problems with use of the chemical. Fishermen knew something was wrong when the fish population in the lake rapidly declined, and housewives could easily identify Lake Volta fish by their smell, but villagers continued to eat the deadly fish. When a connection was made between the illnesses and fish consumption, villagers cut off the heads of the fish and continued to eat the bodies, believing that decapitation would rid the fish of all poison.

Other plants and animals in the lake were killed as well. It was not until the intervention of the Association of People for Practical Life Education, a Ghanian organization, and the blessing of the village witch doctor that the villagers stopped using lindane for fishing and returned to nets and traps. In villages throughout Africa, fishing with pesticides continues where people have not been educated about the safe and effective use of these toxic substances.

the production of new hybrid seeds, developed to produce higher yields with the correct amount of fertilizer and water (70). These laboratory-bred seeds were more susceptible to pests and required increased use of pesticides. Although the new seeds have increased production, the Philippines remains one of the hungriest nations in Asia, according to the Asian Development Bank and WHO (70).

Some years ago, the Farmer’s Assistance Board was formed by peasants and students to study pesticides. The board blames the large volume of pesticide use in the Philippines on the big exporters, as well as on the International Rice Research Institute. The board points to the demand for highest yield and blemish-free products as the reasons for the country’s continued dependence on large quantities of pesticides.

India

The Insecticides Act (1968) and the Insecticides Rules (1971) govern pesticides in India. The Act regulates manufacture, formulation, distribution, and sale of pesticides through a licensing system. Five agencies have been created to implement these laws. Locally generated toxicity and residue data for formulations are required in most instances; however, complete efficacy data are required only for registration of a new pesticide. The Pesticide Registration Committee and the Central Insecticides Board review data for registration, referring to publications and decisions by FAO, WHO, and EPA, among other organizations. India does not adhere to FAO guidelines with respect to labeling. It does follow the FAO color coding of labels based on toxicity, but the warning symbols differ from those suggested by FAO. Pesticides are classified into various categories of toxicity, but the limits set differ from those recommended by WHO (39). To date, 119 active ingredients and their formulations have been registered.

The improper use of pesticides is a major problem in India (5). Few farmers are aware of the potential hazards associated with the use of pesticides (5). Crops are often sprayed with insecticide immediately before and after harvest because of a belief that pre- and postharvest spraying will increase freshness and preservation (5).

India “phase registers” new pesticides. First there is a trials clearance, then a provisional registration, which is valid for 2 years and subject to certain conditions, and finally a full registration. There is also “me-too” registration, which allows a second registrant to obtain registration for a pesticide subject to proof that the product is identical to the one already registered. There is usually a letter of agreement between parties on use of data (39).

The Insecticides Act mandates that pesticide quality be checked by the Central Insecticide Laboratory. Rigid controls are set for preregistration purposes, but once a product is on the market, quality control is not pursued (39). Quality control of products during production is monitored not by the government, but by private companies. Compliance with regulatory policies is enforced by state governments, and imports are allowed only through certain ports of entry (39). No pesticide may be imported without a registration certificate. It is interesting to note that many pesticides which have been banned or severely restricted in the United States are produced in India (70). Several foreign manufacturers have plants in India (70).

Increased agricultural output does not necessarily mean increased food consumption for local residents if the residents are too poor to afford food. Despite the fact that there were vast increases in wheat yields in the Punjab district in the 1960s, the portion of the rural population living below the poverty line increased from 18 to 23 percent (28). While true that pesticide use may increase crop yield and bolster the economy of a developing country, in this particular instance the economic prosperity of the local inhabitants declined.

The Central Food Laboratories monitor pesticide residues and adulterants in food, but this system needs strengthening. State governments are required to obtain reports from their officers on pesticide poisonings, but this is not a thorough monitoring system. Both state and central governments and the pesticide industry have implemented training programs for safe use and application of pesticides (39).

Costa Rica

The Law for the Control of Pesticides (1979) and the Law Governing Occupational Health (1981) regulate pesticides in Costa Rica. Along with other Central American countries, Costa Rica has adopted the provisions of the Basic Document on Regulation of Registration, Marketing and Control of Agricultural Chemicals for Countries of Central America, prepared under the auspices of the Inter-American
Institute for Cooperation on Agriculture in 1985. A Pesticide Commission has also been formed to carry out the pesticide registration program (39).

Registration requirements are generally in accordance with FAO guidelines. Local efficacy data for new products are to be generated either directly by government research organizations or by private companies under government supervision. Efficacy data from other Latin American countries are acceptable for products already registered. EPA tolerances must also be submitted, along with a certificate of registration and a certificate of analysis from the country of origin and evidence of registration from other countries. Labeling is evaluated according to guidelines agreed on under the Basic Document. Full registration is valid for 3 to 5 years, experimental permits are issued, and me-too registration is allowed. As with Mexico and Ecuador, all chlorinated compounds that accumulate in the food chain are banned, but the government reserves the right to use them in cases of emergency when economical substitutes are not available (39).

Costa Rica has one of the strongest enforcement systems in Central America. Import permits are necessary, and there is a licensing scheme for formulation, distribution, and sale of pesticides. The Ministry of Health has done some monitoring of food residues and keeps a record of poisoning cases. The government and private sector carry out training programs for pesticide workers, and the government has published a training manual for physicians.

Mexico

In Mexico, the principal pesticide legislation is the Law on Plant and Animal Protection, which was adopted in 1940. The law was amended in 1974, and rules were added in 1980 to implement it. FAO guidelines are generally followed, with local efficacy data generated either directly by government research organizations or by private companies under government supervision (39). All test protocols must be approved by the government. Emphasis is on evaluation of efficacy data, while toxicological and residue data are reviewed by experts. Label evaluation follows the Basic Document guidelines agreed on by Latin American countries, and the WHO classification system for pesticides has been adopted, with certain modifications (39). Full registration is valid for 3 to 5 years, with permits issued.
for experimental purposes. Me-too registration is allowed with the same data and information requirements as for all registered products.

All chlorinated compounds that accumulate in the food chain are banned, but the government reserves the right to use them in cases of emergency when economical substitutes are not available (39). As recently as 1987, some 28 pesticides that were banned or severely restricted in the United States were being used in Mexico (18). Endrin, which was severely restricted in the United States in 1979, was given a renewal registration for 2 years in 1984 (18). Mexico imports a large percentage of pesticides, but there are also some 300 formulation plants in the country (18). In 1987, domestic production of pesticides was estimated at 32,000 tons per year (18).

The government and private industry share responsibility for quality control, but compliance with regulatory policies is usually enforced only after complaints from the field. Training programs for farmers, distributors, and physicians are sponsored by government and private industry, but monitoring of pesticide poisonings is sporadic. Imports are controlled through the issuance of import permits, and formulation, distribution, and sale of pesticides is controlled through a licensing scheme (39). Residues in export crops are monitored regularly, following regulations imposed by the importing country (39).

Ecuador

In addition to enacting its own legislation in 1984, Ecuador has consented to implement guidelines dealing with registration data and labeling agreed on by Latin American countries in the Andean region. FAO guidelines form the basis for data requirements. Either government research organizations or private companies under government supervision must generate local efficacy data. Further, proof of registration in the country of origin and registration in other countries is required (39).

There is little evaluation of data except for efficacy. Labeling is strictly evaluated, based on the guidelines agreed on by the Latin American countries. Other organizations are looked to for guidance, among them FAO, WHO, EPA, the National Agricultural Chemicals Association, and the International Group of National Associations of Manufacturers of Agrochemical Products.

All chlorinated compounds that accumulate in the food chain are officially banned, but the government reserves the right to use them in cases of emergency when economical substitutes are not available (39). Parathion and toxaphene are two pesticides banned in Ecuador, while DDT and methyl bromide are among those restricted to specified uses. U.S. EPA regulations regarding banning and restrictions are supposed to be closely followed (39), yet DDT, which has been banned by EPA for use in the United States, can be used in certain circumstances in Ecuador.

Both government and private industry have quality control programs. The Fundacion Natura (Nature Foundation), an environmental group, monitors compliance with regulatory policies and reports violations to the government. Government inspectors are also assigned to monitor compliance. The Department of Commerce and the Ministry of Agriculture issue import permits, and there is a licensing scheme for formulation, distribution, and sale of pesticides.

Prior government approval is needed for any pesticide advertising, but there has been minimal
monitoring of residue on food and crops. A record of any poisoning cases reported by hospitals is maintained by the Ministry of Health. Government and the private sector, as well as industry, have training programs for extension workers, farmers, distributors, doctors, and technical and sales representatives.

Kenya

In Kenya, the Pesticide Control Board Act was implemented in 1982, with regulatory authority vested in the Pesticide Control Product Board. The Specialist Approval Committee for Agricultural Pesticides evaluates data generally, in accordance with FAO guidelines. At present, there is no information available concerning labeling requirements, no national residue tolerances, and no system of pesticide classification, although WHO classification is being reviewed for possible adoption. Only registered products can be imported and used, but there are no restrictions regarding the availability of these products (39).

For the most part, quality control is left to industry. Residue monitoring is not usually done, and there is no system in operation for monitoring pesticide poisoning cases (39).

INTERNATIONAL NEUROTOXICOLOGICAL RESEARCH

Active interest in neurotoxicity began in the United Kingdom during and after World War II. Since that time, research efforts in the United States have gradually increased. The United States is now the world leader in environmental legislation and in government funding of neurotoxicology research. Research in other countries has been narrower and more specific. The Scandinavian countries have been active in research on the neurotoxicity of organic solvents (73), and other European countries have supported research on compounds of particular concern in occupational settings, such as pesticides and heavy metals (16,36). In most cases, however, no systematic national effort has been undertaken similar to that in the United States (2).

Several international conferences have taken place during the past 10 years on the subject of neurotoxicology, some of which were sponsored by EPA and the National Institutes of Health. Two international journals published in the United States, Neurotoxicology and Teratology and Neurotoxicology, were established in 1979, and the Society of Toxicology in the United States has a sizable subsection devoted to neurotoxicology. Outside the United States, sufficient interest has been generated in neurotoxicological issues that a new society, the International Neurotoxicology Association, has been formed. This society held its first meeting in 1987, with attendance by approximately 200 scientists from Europe and the United States. The first comprehensive text on neurotoxicology was published in 1980 (52).

Major Directions of Academic, Industrial, and Government Research

In the past, research efforts were often initiated following industrial exposures that caused severe human intoxications. For example, with the advent of the vulcanization of rubber, carbon disulfide poisoning in workers in the rubber industry became common in many European countries (71). With the introduction of rayon, the manufacture of which also required the use of carbon disulfide, poisonings due to use of this solvent became a worldwide problem (68). Improvements in occupational hygiene have largely eliminated cases of severe poisoning; nevertheless, what has emerged instead is the problem of chronic low-level exposures to this and other compounds. The development of human testing procedures to measure more subtle symptoms has been largely accomplished in Finland (49).

The toxicity of lead has been known since antiquity (51). Nonetheless, large-scale lead poisoning continues to be an international public health problem because of lead water pipes, the use of
lead-based paints, and the addition of lead to gasoline. Much of the basic research involving animal models of lead toxicity was done in the United States (67). Using the diagnostic procedures developed for the detection of exposure to organic solvents, Finnish researchers have demonstrated nervous system damage in low-level occupational exposures of adults to lead (49). Research into lead toxicity is still supported enthusiastically in many countries because of accumulating evidence that even exposure levels previously considered harmless (particularly in children) have been shown to have adverse effects on health (ch. 9). This has led the WHO European Office to sponsor a multinational study of the effects of childhood lead intoxication. As of 1989, lead additives have been restricted in the United States and in some parts of Europe. Thus, worldwide interest in lead toxicity continues, although outside the United States research is not supported in a programmatic way by individual governments. It appears that this role has been taken over by international bodies such as WHO.

Another major environmental contaminant is mercury. Exposures to mercury in industrial settings have been well described since the 19th century (34). Mercury became a public health problem because of the widespread use of organic mercury compounds in agriculture as fungicides. The first major outbreak of methyl mercury poisoning occurred in Japan in 1953 and was followed by outbreaks in many other parts of the world, notably Iraq (see ch. 2). Japanese scientists have actively pursued research on the mechanism of neurotoxicity of organic mercury compounds (55). This was followed by a large Scandinavian (mostly Swedish) research effort because of contamination of lakes by mercury runoff (19). U.S. investigators have been involved in mercury research since the Iraq episode, in 1971 to 1972, and have examined such problems as the teratogenic effects of methyl mercury on the behavior of animals (17). Other metals that have been studied internationally include manganese, cadmium, and the organotins.

Interest in the neurotoxicity of organic solvents has increased in recent years. Pioneering work in Scandinavia was followed by mechanistic studies in the United States (47) that revealed the relationship between human symptoms and underlying biological alterations. Scandinavian workers have been the focus of a number of occupational hazard studies. A recent monograph entitled *Organic Solvents and the Central Nervous System* was published jointly by WHO and the Nordic Council of Ministers (73). This document addresses the problems of occupational exposures, the illness caused by these exposures, and the diagnostic procedures for identifying the illness. In 1988, the WHO-Nordic Council of Ministers met to design the “definitive” study of chronic effects of exposure to solvents on the nervous system of workers (75).

The widespread use of highly toxic pesticides has led to intense worldwide research on the neurotoxicity of these compounds. In fact, the beginning of the environmental movement has been attributed to the publication of Rachel Carson’s book *Silent Spring,*
which dealt with the ecological effects of indiscriminate pesticide application. The continuing development of new pesticides has caused the research effort to be sustained, not only to protect human populations, but also to safeguard nontarget populations from inadvertent exposure to these compounds.

One way to document international research trends is to summarize the distribution of research papers published by non-U.S. authors in the two international journals devoted to neurotoxicology. Table 9-1 indicates the various neurotoxic substances investigated in papers published in two journals between 1979 and 1987.

Heavy metals as a group clearly represent the major area of interest. They are followed by organic solvents, pharmaceutical agents, and pesticides. Since the two neurotoxicology journals are relatively new, one can assume that a large proportion of neurotoxicological research has also been published in other journals. In addition, each of the non-English-speaking countries listed has journals in its own language, and researchers also publish in those journals. This is particularly true of scientists in the Soviet Union, who publish only infrequently in English-language journals. Thus, while this survey of published research outside the United States may not be truly representative of international neurotoxicological research, it is probably a reasonable indicator of general trends in international research.

To gain another view of current research trends, it is useful to examine projects presented at the first meeting of the International Neurotoxicology Association in the Netherlands, May 10-16, 1987. The meeting was attended by 135 scientists from 21 countries. The largest contingent came from the United States (23), followed by the Netherlands (20), West Germany (15), England (11), Italy (11), and all other countries (fewer than 10 each). An examination of their places of employment indicates that 37 percent of the attendees were from government laboratories, 37 percent from academia, 23 percent from industry, and the remainder from a variety of institutions. Of the U.S. participants, 22 percent were from government laboratories, 65 percent from academia, and 9 percent from industry. An examination of the topics presented indicates that the trends outlined above have not changed markedly (table 9-2). Following tradition, 50 percent of the papers dealing with solvent toxicities came from Scandinavian countries.

<table>
<thead>
<tr>
<th>Country</th>
<th>Substances investigated (No. of papers)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Canada</td>
<td>Ethanol (3); manganese (2); cadmium (2); lead (2); pharmaceutical agents (2); acrylamide (1); zinc (1); aluminum (1); herbicides (1); hydrogen peroxide (1); chlorinated hydrocarbons (1)</td>
</tr>
<tr>
<td>England</td>
<td>Pyrethrins (7); pharmaceutical agents (7); organophosphates (2); solvents (1); acrylamide (1); mercury (1); herbicides (1)</td>
</tr>
<tr>
<td>Italy</td>
<td>Pharmaceutical agents (8); organophosphates (2); mercury (1); solvents (1); bismuth (1); caffeine (1)</td>
</tr>
<tr>
<td>India</td>
<td>Manganese (4); organophosphates (1); lead (1); cadmium (1); solvents (1); sulfur dioxide (1); zinc (1); styrene (1); herbicides (1)</td>
</tr>
<tr>
<td>Japan</td>
<td>Mercury (5); solvents (3); cadmium (1); pyrethron (1); pharmaceutical agents (1)</td>
</tr>
<tr>
<td>France</td>
<td>Mercury (3); solvents (1); tellurium (1); lead (1)</td>
</tr>
<tr>
<td>Mexico</td>
<td>Solvents (6)</td>
</tr>
<tr>
<td>Finland</td>
<td>Lead (4); solvents (4); ethanol (1)</td>
</tr>
</tbody>
</table>

**SOURCE:** Office of Technology Assessment, 1990.

**Table 9-2-Subjects of Neurotoxicological Research Presented at a Major International Conference**

<table>
<thead>
<tr>
<th>Chemical</th>
<th>Papers (No.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insecticides</td>
<td>25</td>
</tr>
<tr>
<td>Solvents</td>
<td>23</td>
</tr>
<tr>
<td>Lead</td>
<td>8</td>
</tr>
<tr>
<td>PCBs</td>
<td>2</td>
</tr>
<tr>
<td>Acrylamine</td>
<td>2</td>
</tr>
<tr>
<td>Methyl mercury</td>
<td>1</td>
</tr>
<tr>
<td>Styrene</td>
<td>1</td>
</tr>
<tr>
<td>Carbon monoxide</td>
<td>1</td>
</tr>
<tr>
<td>Nitrous oxide</td>
<td>1</td>
</tr>
<tr>
<td>Nitrous oxide</td>
<td>1</td>
</tr>
<tr>
<td>Pharmaceutical agents</td>
<td>4</td>
</tr>
<tr>
<td>Experimental compounds</td>
<td>6</td>
</tr>
</tbody>
</table>

**SOURCE:** Office of Technology Assessment, 1990.

One meeting may not represent a typical sample of international research in neurotoxicology, but it provides a useful example of current neurotoxicological research in the Western industrialized world. No researchers from the Soviet Union attended this meeting; however, two individuals from Eastern Europe, one each from Hungary and Czechoslovakia, attended. The number of neurotoxicologists in both of these countries is very small, as determined by publications in the literature. For much of the rest of the world, neurotoxicology as a discipline does not exist. There are some exceptions, however. For example, there are active researchers in Japan, India, China, and Argentina, with well-identified centers for such research. Indian researchers have traditionally published in English, and this practice is becoming increasingly common among Chinese researchers as well. In addition, experimental re-
search on the neurotoxicity of the grass pea is now under way in Ethiopia.

**Neuroepidemiology**

International activities in neuroepidemiology have taken place on all six inhabited continents. Neuroepidemiologists in England are currently studying risk factors for stroke and are investigating the epidemiology of multiple sclerosis. In Japan, epidemiological inquires into the etiology of neurodegenerative disorders (including amyotrophic lateral sclerosis, Parkinson’s disease, Alzheimer’s disease) have been undertaken. One country with a major effort in neuroepidemiology is Italy. Italian efforts in this area may be traced back to a series of courses on neuroepidemiology taught in 1979 by a group of U.S. and Italian epidemiologists. The fruits of these efforts have included major work in the epidemiology of dementia. More recently, WHO has begun an international initiative in the epidemiology of dementia. It is not clear, however, whether this work will be extended to other neurodegenerative conditions. It is possible that some of these efforts will be focused on geographic isolates of neurological conditions, for example, the Faroe Islands and multiple sclerosis, Guam and dementia, and Guam and amyotrophic lateral sclerosis. An international collaboration to investigate the latter two phenomena is now forming and will likely begin its activities within the next year (31).

**International Cooperation**

Neurotoxicological research has been primarily an intranational effort. In recent years, some international cooperation has been initiated by WHO and the U.S. National Toxicology Program, but thus far this has occurred only in specific areas, such as lead toxicity, solvent toxicity, and the development of testing methodologies (74). The limited scope of international cooperation is largely due to the lack of funds available for such efforts.

**Comparison of U.S. and Foreign Research Programs**

The neurotoxicity research effort in the United States is larger in depth and scope than that in other nations. Both leading books in this area were written by American authors and editors (4,52). Both international journals in the field are published in the United States, and a review of the published literature in neurotoxicology reveals that about 90 percent originates in the United States. The quality of the work is generally considered to be excellent. As mentioned previously, other countries have excelled in some areas of research; this is particularly true with respect to the solvents research conducted in Scandinavia. American research on the mechanisms of toxicity of solvents is generally considered to be outstanding.

**Resources**

The United States has a limited number of doctoral-level training programs in neurotoxicology. Because of its unique educational system, more scientific manpower is available in the United States than in other countries. In most European countries, the standard educational program in the life sciences is the medical degree, or the equivalent of the M.D. Consequently, almost all researchers in Italy, Scandinavia, and Germany are trained first as physicians and then as researchers. These individuals may eventually obtain a doctorate if they choose a research career. In countries such as Italy, where research positions are very difficult to obtain, most physicians choose nonresearch careers rather than risk being unemployed. Although employment opportunities are somewhat better in Scandinavia than in Italy, it is still difficult to establish a research career because of the scarcity of positions.

The success of the American research enterprise is due not only to the relative availability of funding, but also to the manner in which the funds are administered. Despite some inherent flaws, the peer review system in the United States generally ensures that the best scientists in a given field obtain funding. In many other parts of the world, research is often supported by a system in which funding decisions are made solely by the director of an institute or the chairman of a department, without peer review of the proposed research.

**Future Directions**

A recent review (1) listed 850 chemicals in the workplace that may be neurotoxic. Apart from the substances listed in tables 9-1 and 9-2, most of these chemicals have not been studied. The international chemical industry produces several thousand new chemicals every year, most of which are not tested for neurotoxicity. Japan and France now require neurotoxicity testing for new chemicals (53), but these tests are elementary in nature and are likely to miss more subtle and insidious toxic effects.
At present, the major classes of neurotoxic substances—heavy metals, solvents, and pesticides—have been identified. However, despite major research efforts, there is still no clear understanding of the mechanisms of toxicity of most of these chemicals. In order to protect human populations from chronic low-level intoxication, it is essential to understand the properties and potential health effects of new and existing chemicals. Because of the enormity of the testing task, a coordinated international approach would be highly beneficial.

**Foreign Governments Likely To Take Leadership Roles**

In some European countries, notably West Germany and Sweden, environmental movements are becoming increasingly influential. It is likely that these nations will play leading roles in supporting research and in developing regulations to control toxic substances. The Federal Republic of Germany has already acted to remove lead from gasoline and to fund studies of lead toxicity in children. As outlined above, all of the Scandinavian countries (Sweden, Denmark, Norway, and Finland) have traditionally supported research on solvents. These patterns are likely to continue and may broaden to the investigation of other agents as environmental movements grow. Political events in the Soviet Union have led to the emergence of an environmental movement, and it appears that the Soviet government will also take a more active role in these issues. In the Far East, both the People’s Republic of China and Japan are faced with major pollution problems and are becoming increasingly involved in toxicological issues.

**SUMMARY AND CONCLUSIONS**

Like most environmental concerns, neurotoxicity is a problem not limited by national boundaries. Pollutants can readily cross national borders, hazardous chemicals are frequently imported and exported among both industrialized and developing nations, and adulterated food and commercial products enter the United States despite current regulatory efforts. Strategies to limit human exposure to neurotoxic substances should be devised in the context of both national and international regulatory and research initiatives.

Despite numerous regulations governing the export and import of neurotoxic chemicals and products containing them, most countries do not adequately protect human health and the environment from these substances. Most industrialized nations have policies and procedures in place to regulate the import, distribution, and use of toxic chemicals, implicitly including neurotoxic substances. Some developing nations have limited regulations to protect workers and consumers from the adverse effects of neurotoxic substances. Developing nations that do have regulations often do not have the resources to enforce them. Developing countries use only 10 to 25 percent of the world’s pesticides, but they account for as much as 50 percent of the acute poisonings of pesticide applicators and between 73 and 99 percent of their deaths. This lack of effective regulation and enforcement in developing nations has a negative impact not only on public health and environment in the user country, but also in industrialized nations, including the United States, where people process and consume pesticide-treated crops imported from developing nations.
Both TSCA and FIFRA contain provisions exempting certain products produced for export from the requirements that apply to products sold for use in the United States. In most instances, TSCA requirements do not apply to substances manufactured, processed, or distributed for export. The requirements do, however, apply if it is determined that the substance will present an unreasonable risk of injury to public health or the environment within the United States. In addition, because pesticides intended solely for export are exempt from the public health protection provisions of FIFRA, pesticide manufacturers can legally export banned, severely restricted, or never registered substances that have been deemed too hazardous for use in this country. Companies that do so are required to notify the importing country that the exported pesticides have been banned, severely restricted, or never registered for use in the United States. Some such pesticides are used on food crops that are imported back into the United States for consumption. Critics of this practice have termed it the ‘circle of poison.

On January 15, 1981, several days before the end of his term, President Jimmy Carter issued an Executive Order which put controls on exports of substances that were banned or severely restricted in the United States. Several days after Ronald Reagan became President, he revoked the order.

While pesticides may be needed to obtain sufficient food to feed the ever-increasing world population, many observers argue that ample food supplies are currently available and that better distribution of existing food stores is necessary. Responsible conduct on the part of persons who manufacture, distribute, and use pesticides is mandatory if irreversible harm to world public health and the world environment is to be minimized. Education and literacy levels of persons handling pesticides must be considered and appropriate information tailored to their needs. Regulations currently in place must be adhered to and new legislation enacted when the need arises. Alternative methods of pest control should be investigated and developed. Cooperative efforts on the part of governments in industrialized and developing countries, industry, environmental groups, and other international organizations are necessary to ensure the safety of the world community.

Active interest in neurotoxicity began in England during and following World War II. Since that time, efforts in the United States have gradually increased. Today, the United States is the world leader in environmental legislation and government funding of neurotoxicological research. The Scandinavian countries have been active in research on the neurotoxicity of organic solvents. Other European countries have supported research on compounds of particular concern in occupational settings, such as pesticides and heavy metals.

International research activities tend to focus on the heavy metals (lead and mercury), organic solvents, and pharmaceutical agents. Foreign neurotoxicology-related scientific papers published in international journals most often originate from authors in Canada, England, Italy, Australia, and Japan. A number of papers originate from authors in France, India, Sweden, Finland, and Mexico, as well.

International cooperation in the neurotoxicology field is very limited. Neurotoxicological research has been primarily an intranational effort. In recent years, some international cooperation has been initiated by WHO and the U.S. National Toxicology Program, but thus far this has only occurred in specific areas, such as lead toxicity, solvent toxicity, and the development of testing methodologies. The limited scope of international cooperation is largely due to the lack of funds available for such efforts.

In some European countries, notably the Federal Republic of Germany and Sweden, environmental movements are becoming increasingly influential. It is likely that in the future these governments will play leading roles in supporting research and in developing regulations to control toxic substances. The Federal Republic of Germany has already acted to remove lead from gasoline and to fund studies of lead toxicity in children. All of the Scandinavian countries have traditionally supported solvent research. This will likely continue and may broaden to include the investigation of other agents as environmental movements grow.

**CHAPTER 9 REFERENCES**

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