REGULATORY AGENCIES

1. Overview

The purpose of Earth Day is the recognition that the environment, including all living things, must be protected. The first Earth Day, April 22, 1970, also marked the beginning of more concentrated attempts to develop regulations covering health, safety, and environmental issues; this effort is still underway today.

Regulations change continuously with updates and reauthorizations, and the specifications of these regulations quickly become outdated. Therefore, the discussions in these articles on regulatory agencies provide only an introduction and summary of the U.S. Federal laws and regulations covering health, safety, and environmental issues. These articles should not be used in lieu of legal services. Current copies of the laws and regulations must be consulted in order to deal with specific situations. Many of the laws and regulations can be accessed on the Web, citations are noted throughout this article.

The two main federal agencies involved in the protection of the environment and human health are the Environmental Protection Agency (EPA) and the Occupational Safety and Health Administration (OSHA). The EPAs principal concern is the protection of the environment, in most cases, the area outside of an industrial facility. Primary laws covered by EPA are the Clean Air Act Amendments (CAAA), the Clean Water Act (CWA), Resource Conservation and Recovery Act (RCRA), Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA), Toxic Substances Control Act (TSCA), and Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA).

The principal function of OSHA is the protection of people, eg, employees, visitors, and temporary help, in the workplace. The principal law covered by OSHA is the Occupational Safety and Health Act (OSHA). There are 10 regional offices that carry out the regulatory functions of both EPA and OSHA (www.epa.-gov/epahome/aboutepa.htm#regiontext).

There are a number of other federal agencies involved in related work. Pertinent agencies and their areas of concern are listed in Table 1. The control of the manufacture, use, and exposure to hazardous or toxic chemicals is mainly divided between EPA and OSHA. In addition, the Food and Drug Administration (FDA) has control over chemicals in food, drugs, and cosmetics. The Consumer Product Safety Commission (CPSC) is concerned with the safety of all consumer products, including child-resistant packaging regulations. The U.S. Department of Agriculture (USDA) maintains strict controls over chemicals in food, as well as "gene-modified" food. The specific concerns and requirements of these various laws are considered in detail in the regulatory agency articles pertaining to the specific industries. Additionally, the Department of Transportation (DOT) regulates the handling and transport of materials, including chemicals, by highway, rail, air, and water. Regulations cover training requirements for transporters, types of containers that can be used, labels and placards, incident reporting, etc (see TRANSPORTATION).

In addition to the federal agencies, there are many state, as well as county and municipal agencies, that regulate the environmental and health areas. When state regulations are not as stringent as federal regulations, the federal rulings may take precedence. International laws and regulations must also be

taken into account. International transportation requirements can affect shipments of products and raw materials. The use of products can also be affected by international rules.

The difference between laws and regulations is important. For the former, the U.S. Congress first passes a bill, which is then signed by the President, and thereby made a law or act. The act describes what Congress wants regulated, the general method to be used, and the ultimate results expected. It is then the responsibility of the designated agency to write and administer regulations to meet these requirements. First, the agency issues draft regulations that are mainly for internal review. It also tries to obtain the response of the affected portions of the public and industry. Next, proposed regulations are published in *The Federal Register* (on-line information at http://www.access.gpo.gov/su_docs/aces/aces140.html), a daily document published by the General Services Administration. A specific comment period is allowed, during which public hearings may be held. The Office of Management and Budget also reviews the regulation, mainly to determine the financial impact of the regulations on industry. Once the comments are received and revisions are made, the final regulations are published in *The Federal Register*. Every few years, Congress reviews a particular law and its regulations to see how well it is working. At that time, it can be amended, or reauthorized, to make any improvements.

The Federal Register contains, in addition to proposed and final regulations, notices for all of the federal agencies. Twice a year, usually in April and October, the Unified Agenda is published in *The Federal Register*, listing all regulatory activities, from preproposed activities through proposed and final rulemaking. Expected dates for action are given.

Regulations are compiled and listed by agency in the *Code of Federal Regulations* (CFR). The CFR is divided into 50 titles. EPA regulations are in Title 40 while OSHA regulations are listed under Title 20. The listing first gives the number for the agency, then CFR, and then the part, or chapter, and number. An example is the EPA regulations on National Primary and Secondary Ambient Air Quality Standards: 40 CFR 50. *The Code of Federal Regulations* may be accessed on-line at http://www.gpo.access.gov/cfr/index.html. EPA laws, regulations, etc, can be found on-line at http://www.epa.gov/epahome/rules.html. OSHA laws, regulations, etc, can be found on-line at http://www.osha.gov/fso/ca.html.

The applicability of many of the government regulations were originally based on the Standard Industrial Classification (SIC) of the process and/or facility, which is also known as the SIC Code and is assigned for tax and financial purposes. Because the classification can determine if a facility falls under certain regulations, it is important to ensure that the classification is correct. The SIC Code consists of four digits, the first two of which show the principal group. For chemicals and allied products, this group is 28. The SIC Code was replaced by the North American Industry Classification System (NAICS) in 1987. NAICS was developed jointly by the U.S., Canada, and Mexico to provide new comparability in statistics about business activity across North America. The official website for the NAICS is http://www.census.gov/epcd/www/naics.html. This is the link to the NAICS list: http://www.census.gov/epcd/naics/naicscod.txt. And

this is the link to a comparison of the SIC Codes and the NAICS: http://www.census.gov/epcd/www/naicstab.htm.

An important aspect of environmental, health, and safety laws and regulations is enforcement. Federal, state, and local regulatory authorities tend to have large enforcement sections. In the environmental area, compliance audits are usually conducted annually. OSHA, both federal and state, often audit based on a facility's accident/incident rate.

Penalties for noncompliance are based on the severity of the violation, but is typically $25,000/day for each day of noncompliance. When a noncompliance is deemed to be willful, ie, the company knew they were committing a violation, the penalty can include a jail term in addition to the fine. When people or the environment suffer damage, a company can be sued as well.

2. U.S. Food and Drug Administration

The U.S. Food and Drug Administration (FDA) is the primary federal scientific and regulatory government agency that monitors drug, biologic, medical devices, food, veterinary, and cosmetic products. It has been estimated that Americans spend approximately 25 cents of every dollar on FDA-regulated products (1). FDA employs approximately 9500 people, of whom chemists are the second most numerous, totaling over 1100 persons. Among the other technical personnel that compose the core of the agency are physicians, pharmacists, pharmacologists, biologists, toxicologists, microbiologists, and statisticians.

FDA's mission has traditionally been consumer protection. However, the manner in which the agency accomplishes its regulatory mission has been changing with the explosion of advances within analytical chemistry and toxicology. Because new and better compounds are continuously being developed, increased attention is being devoted to the dilemma of speeding their entry into the market while ensuring their safety and effectiveness. Scientists must not only develop new compounds, but also explain how the benefits outweigh the risks so that society can benefit from their work. Because no compound is completely safe, FDA must make an assessment of the intended use and determine whether the level of risk is acceptable. Only when FDA is able to make timely, scientifically based judgments on data will society reap the rewards of science. For example, FDA has taken the position that society is willing to accept a higher degree of risk for a life-saving device or drug than for a cosmetic or food additive. Making these judgments in a scientific and political context is the responsibility of FDA.

As a regulatory agency staffed by scientists making decisions on a daily basis, FDA's obligations are significant from both a health and safety and an economic perspective. The quality of the scientific expertise both within the FDA and relied on by the agency plays a key role in each and every FDA decision.

2.1. FDA Organization and Roles. The FDA is headed by the Commissioner of Food and Drugs [Office of the Commissioner (OC)]. This position is not a Cabinet-level office but falls within the Public Health Service (PHS), a division within the U.S. Department of Health and Human Services (HHS). The post of FDA Commissioner is subject to HHS political clearance and Senate

confirmation, and the Commissioner is ultimately accountable to HHS, Congress, and the President of the United States. The Commissioner has a staff to assist in policy making and several deputy commissioners to oversee operation of all the subordinate units. FDA has six regional offices within the country, each responsible for a section of the country, and 21 district offices. Persons with technical background typically work in one of FDA's chemistry laboratories or as investigators or consumer safety officers.

The FDA's approval and enforcement programs are administered by five centers organized along product lines. Although all five centers must follow the general provisions of the Act, each center is governed by its own unique and distinctive set of laws and regulations. The five centers are as follow.

(*1*) Center for Drug Evaluation and Research (CDER). This center is responsible for the regulation and approval of all branded and generic human drugs, including prescription, over-the-counter, and antibiotic drugs. A drug is defined by the Act as an article intended either to be used in the diagnosis, cure, prevention, mitigation, or treatment of disease in humans or animals, or to affect the structure or any function of the body (2).

(*2*) Center for Biologics Evaluation and Research (CBER). This center is responsible for the regulation and approval of all biological products intended for use in the treatment, prevention, or cure of diseases or injuries to humans. A biological product is any virus, therapeutic serum, toxin, antitoxin, vaccine, blood or blood component or derivative, or analogous product (2). It also includes products produced by biotechnology, such as interferons and erythropoietins.

(*3*) Center for Devices and Radiological Health (CDRH). This center is responsible for the regulation and approval of medical devices as well as such products as x-ray machines and color television sets. A medical device is defined as an instrument, apparatus, implement, machine, contrivance, implant, *in vitro* reagent, or any related article intended either for use in the diagnosis of conditions or the diagnosis, cure, treatment, mitigation, or prevention of disease, or to affect the structure or any function of the body (2). Medical devices are distinguished from drugs in that devices do not achieve their primary intended purpose through chemical action in the body and need not be metabolized.

(*4*) Center for Food Safety and Applied Nutrition (CFSAN). This center is responsible for the regulation and approval of food for human consumption, food additives, color additives, and cosmetics. Although CFSAN does not regulate meat and poultry, it does set safety and sanitation standards for supermarkets, restaurants, and other retail food establishments.

(*5*) Center for Veterinary Medicine (CVM). This center is responsible for the regulation and approval of animal food and drug products. The center also ensures that animal drugs and medicated feeds are safe and effective and that food from treated animals is safe to eat.

Also included in the basic structure are National Center for Toxicological Research (NCTR) and the Office of Regulatory Affairs (ORA).

Independent of these centers, the FDA also has overlapping jurisdiction with several other federal agencies, including the U.S. Department of Agriculture; the Bureau of Alcohol, Tobacco, and Firearms; the Federal Trade Commission; and the Environmental Protection Agency.

Most (~90%) of the FDA's work involves enforcement of the Act. Its consumer protection function includes premarket approval and quality standards for drugs and medical devices, factory inspections, and market surveillance. FDA can combat transgressions such as the mislabeling of drugs or the adulteration of foods by issuing press releases and/or warning letters, seizing products, recommending criminal prosecutions of violators to the Department of Justice, or seeking injunctions in federal courts against companies that manufacture or ship products which do not meet legal or regulatory standards necessary for consumer safety.

Because each center has its own rules and regulations, the best way to understand FDA's regulatory role is to review FDA's regulation of drug, biologic, medical device, food, veterinary, and cosmetic products separately (3).

3. Regulation of Pharmaceuticals, Cosmetics and Food

3.1. Regulating Drug Products. The FDA has the authority to regulate new drugs from early laboratory research through clinical testing and market approval. In order to be approved for marketing, a new drug must be shown to be both safe and effective for its intended use (4). Safety means a low incidence of adverse reactions or insignificant side effects under adequate directions for use and warnings; it also means low potential for harm which may result from abuse under stated conditions or widespread availability. Effectiveness means a reasonable expectation that the pharmacological effect of the drug will provide clinically significant relief of the type claimed for that drug in a significant proportion of the target population when used with proper directions and warnings.

The FDA new drug approval process, which is the way most products enter the market, begins with clinical investigations. However, before clinical investigations can commence, FDA requires significant preclinical investigations involving tests on laboratory animals. These tests are to determine the nature of the chemical and to establish evidence concerning the toxicity of the substance. If, through animal studies, the drug is determined to be safe enough for human experimentation, an Investigational New Drug (IND) Application must be submitted to the Center for Drug Evaluation and Research before beginning human clinical trials. No human clinical studies may be started until 30 days after FDA has been notified.

FDA's control of clinical drug investigations is derived from the Act's prohibition of the shipment of an unapproved new drug in interstate commerce. The Act also specifically authorizes FDA to require INDs. Accordingly, FDA has implemented IND regulations that shape and control IND investigations (5). Additionally, regulations regarding the rights of human subjects, informed consent, the sale of investigational drugs, and the obligations of sponsors, monitors, investigators, and Institutional Review Boards (IRBs) have also been adopted to implement the statutory IND language (5).

Clinical investigations are broken into three phases, all of which are conducted under the oversight of an IRB to ensure that appropriate safeguards exist to protect the rights and welfare of the research subjects. The first phase

of clinical investigation involves the initial administration of the drug to a small number of healthy human subjects in order to test for toxicity, drug metabolism, absorption, elimination, administration, safe dosage, and other pharmacological information. The second phase covers trials using a limited number of patients for specific disease control or for assessing diagnostic, prophylactic, or other medical use. Tests in this phase usually consist of several hundred patients and take up to two years. Less than one third of the drugs that begin the IND process typically proceed beyond this stage, usually because of safety concerns. The third phase entails large-scale clinical trials on individuals with the relevant condition. These trials can begin only if the data generated in the first two phases provide reasonable assurance that the drug is safe and effective. The third phase is intended to document safety, effectiveness, optimal dosage schedule, side effects, and directions for use in the treatment or prevention of the disease or condition. FDA typically meets with the drug firm throughout clinical trials in the third phase to identify special problems and additional testing that might be needed.

After all clinical trials are completed, the sponsor of the drug submits a New Drug Application (NDA) to FDA. The NDA consists of the IND data, manufacturing information, and data on drug stability (6). To facilitate timely review, FDA classifies all NDAs according to their therapeutic potential as compared to previously marketed drugs. Type A indicates therapeutic gain; Type B, modest therapeutic gain; Type C, little or no therapeutic gain; and Type D, both therapeutic gain and risks. Drugs proposed for use in AIDS treatments are classified as I-AA for priority review.

In order to be approved, an NDA must include data which demonstrate that the drug is both safe and effective. Each NDA is assigned to a division within CDER for consideration and administrative control, and then assigned to the appropriate therapeutic group within the division for review. The primary team of reviewers typically consists of a physician, a pharmacologist or toxicologist, and a chemist.

Other offices within CDER may become involved in the review process via consults. For example, the Office of Epidemiology and Biostatistics analyzes statistical data, the Office of Research Resources provides bioavailability reviews, and the Office of Compliance determines from the results of inspections whether the firms meet FDA's Current Good Manufacturing Practice (cGMP) regulations. Advisory committees composed of independent experts are often asked to meet and further analyze the data. Often they also advise as to what additional data and information may be needed. After FDA's review is completed, FDA issues either a Summary Basis of Approval (SBA) for the drug or a recommendation against approval. If approved, FDA releases the SBA and a summary of the safety and effectiveness data to the general public.

Regulating drug quality is a federal concern that is reflected beyond the approval process. FDA has implemented extensive regulations to ensure that drug products that are produced and marketed, as well as their chemical constituents, continue to meet high standards of quality, purity, and safety, and have the identity and strength accurately represented.

The most far-reaching program for ensuring the quality of marketed drug products is the system of cGMP regulations (7). The cGMP requirements are

enforced at two stages of the development and marketing of pharmaceuticals. FDA will refuse to approve an NDA if it determines that the proposed methods, facilities, and controls are inadequate to preserve the identity, strength, quality, and purity of the drug. Once a new drug is approved, the cGMP requirements are enforced through a system of FDA inspections of manufacturing establishments.

Several classifications exist within the broad category of pharmaceuticals, each of which has its own definition and form of regulation. For example, there is a special regulatory category for drugs that are intended to treat rare diseases or conditions, ie, orphan drug products. Because the development of these drugs cannot be economically viable without some form of government assistance, Congress has passed legislation to provide incentives for drug manufacturers to develop these drugs. These incentives include a period of marketing exclusivity for approved drugs that obtain orphan status, as well as U.S. tax credits and possible direct government financial assistance.

Another distinct class of drugs are those requiring a prescription or a written order from a physician or health professional. Congress authorized FDA to determine whether a drug should be a prescription drug. Typically prescription drugs are those that (*1*) have habit-forming characteristics; (*2*) require a physician's supervision, because of toxic or other harmful effects, methods of use, or collateral measures necessary for use; or (*3*) are limited to prescription use under an NDA.

Drugs which are available without a prescription are readily available to consumers over-the-counter (OTC) (8). An OTC drug is low in toxicity, has low potential for harm, can be labeled for safe use without a doctor's supervision, is not habit-forming, and can be taken under easily understood conditions. The Act distinguishes between new drugs and those that are generally recognized as safe and effective. Because many OTC drugs have been marketed for years, FDA has subjected most OTC drugs to a significantly less restrictive set of regulations. This result stems from the statutory and pragmatic view that, given the agency's limited resources and the lesser hazards associated with OTC products which are generally used to alleviate symptoms rather than treat diseases, OTC products require less review. Therefore, most OTC drugs are excluded from new drug status, and no NDA has to be submitted if the active ingredient or combination of active ingredients is found to be safe and effective by the FDA as announced in final OTC drug regulations, and if the labeling of the product conforms to these OTC drug regulations.

Another subcategory of drugs are those that are reviewed under the Abbreviated New Drug Application (ANDA) process (9). These drugs are usually called generic drugs. A generic drug is one that is equivalent to a pioneer or brand-name drug but is not marketed until the brand-name drug's patent and exclusivity periods have expired. Until the 1984 Amendments, all manufacturers trying to market a new drug were required to generate their own data supporting the safety and effectiveness of their versions of the product, even if a drug with an identical active ingredient had already gone through the NDA process. The 1984 Amendments allowed generic drugs to be approved on the basis of abbreviated NDAs (ANDAs). This abbreviated approval process has the dual purpose of getting safe, effective, and less expensive generic drugs on the market, and of

extending the term of patent protection to pioneers in recognition of the need for original research by pharmaceutical companies.

Although generic drugs must meet the same standards as new drug products for identity, strength, purity, stability, adequate labeling, and bioequivalence, they need not go through the extensive clinical trials of a NDA. Instead, these generic drugs must show bioequivalence to the pioneer drug and fall into acceptable parameters set for bioavailability, which is the extent and rate at which the body absorbs the drug. By reducing the testing time, the cost of bringing the drug to market can be reduced by millions of dollars.

Finally, a different set of rules is applied to antibiotics and insulin-containing drugs (10). These categories are regulated under a monograph system mandated by statute. Thus, when a drug in these categories has been demonstrated to be safe and effective to the satisfaction of FDA, the agency promulgates a regulation of general applicability, describing in detail the required specifications of the drug. Thereafter, manufacturers meeting the standards in that regulation may obtain FDA clearance for their own product without submission of any data on safety and effectiveness, other than data demonstrating bioequivalence to the original product. Thus, later versions of a monographed antibiotic or insulin drug product are treated in a manner similar to generic drugs. Another historic distinguishing feature of this category of drugs was the requirement of batch certification. Under this requirement, the manufacturer would submit a sample from a batch of its product to FDA for testing to ensure that the batch meets the stated potency value. The batch requirement was eliminated by FDA in 1982.

3.2. Regulating Biological Products. The process for gaining FDA approval for a biological product is similar to that for a drug product. The FDA regulations require that the person or entity, eg, manufacturer, sponsoring or conducting a clinical study for the purpose of investigating a potential biological drug product's safety and effectiveness submit an IND to the Center for Biological Evaluation and Research. Clinical trials are subject to IRB review, just as drug studies. After completing the IND studies, the manufacturer submits the safety and effectiveness data generated by the studies to FDA in the form of a product license application (PLA). It is the responsibility of FDA to review the proposed labeling, the preclinical (animal and laboratory) data, the clinical (human testing) data, as well as the facilities utilized and the methodologies employed in the manufacture of the product to determine whether the product is safe and effective for its intended use. Biological products are unique in that, in addition to receiving approval of a PLA, the establishment manufacturing the biologic is subject to a prelicense inspection of the facility and the processes used to produce the potential licensed product. If both product and facility meet all standards and regulations, FDA will approve a PLA for the product and an establishment license application (ELA) for the facility (11).

3.3. Regulating Medical Devices. A person or company engaged in the manufacture, preparation, compounding, assembly, or processing of a device intended for human use must follow the regulations enforced by FDA's Center for Devices and Radiological Health. The level of FDA regulation or control is governed by the class in which the device is placed by the agency, ie, Class I, II, or III (12). Class I devices are those requiring the lowest level of regulation

and are subject to general control requirements. These general controls include establishment registration; device listing; premarket notification, ie, 510(k), submission; and cGMP requirements. Class II devices are subject to special controls as well as the general control requirements. Special controls may include labeling and mandatory performance standards or other requirements. Class III devices are subject to general controls and cannot be marketed until they have an approved Premarket Approval Application (PMA) or, as a result of premarket notification (510(k)) submission, until they have been found by FDA to be substantially equivalent to preamendment devices.

Unless otherwise exempt, a firm must submit a premarket notification, also called a 510(k), to the FDA 90 days before it intends to market a device for the first time (13). The 510(k) submission must contain sufficient information to show that the device in question is substantially equivalent to a legally marketed device for a particular intended use. This notification is also required for a product when there is a change or modification to a product that may significantly affect the safety or effectiveness of the device, or when there is a significant change or modification to the intended use of the device.

Class III devices, unless they are substantially equivalent to a device already marketed without a PMA application, require formal FDA approval through the PMA process before initial sale. The PMA process is comparable to the new drug approval process (14). In both cases, safety and effectiveness data must be reviewed by FDA prior to marketing. An approved PMA application acts like a private license granted to the applicant to market a particular device. Other firms seeking to market the same type of device for the same use must also have an approved PMA.

PMA requirements differ between preamendment and post-amendment devices. Preamendment devices are those in commercial distribution before May 28, 1976; post-amendment devices are those first commercially distributed after the date. Class III post-amendment devices that are not substantially equivalent to preamendment Class III devices are considered new devices. Manufacturers of such devices are required to obtain PMA application approval before marketing these. If the post-amendment device is substantially equivalent to a preamendment device and FDA has not initiated a regulatory process specifically requiring the submission of a PMA for the device category, a 510(k) submission can be made.

To allow manufacturers to develop clinical safety and effectiveness data on devices requiring a PMA submission, FDA has implemented regulations that exempt devices intended solely for investigational use from certain provisions of the Act. This exemption is known as the Investigational Device Exemption (IDE) and allows manufacturers of devices intended solely for human investigational use to ship these products through interstate commerce (15). Like the IND regulations, the IDE regulations shape and control the investigational research. If a device is not considered to present a significant risk, an IDE submission to FDA is not necessary. If a device is considered to present a significant risk, an IDE application must be submitted to FDA for approval. In both cases, patient informed consent and IRB approval and oversight is required.

Every device manufacturer, regardless of the device class, must adhere to the requirements set forth in the device cGMP regulations (16). The essential

objective of the cGMP regulations is to create a quality assurance system so that the finished device meets all the necessary specifications to maintain a high manufacturing standard. The cGMP regulations cover the methods, facilities, and controls used in preproduction design validation, manufacturing, packaging, storing, and installing medical devices. FDA monitors compliance with the cGMP regulations during its inspection of the firm's manufacturing facilities. To address the variety and complexity of devices, the cGMP regulations designate two device categories: noncritical and critical. General requirements apply to all devices, and critical devices must meet additional cGMP requirements.

3.4. Regulating Food Products. The mandate of the Center for Food Safety and Applied Nutrition (CFSAN) includes U.S. food processors, dietary supplement manufacturers, food warehouses, and cosmetic products. U.S. food processors spend $1.4 billion annually on research and development and introduce 10,000 new grocery products each year. CFSAN monitors over 3000 food additives, thousands of pathogens, and hundreds of pesticides. In addition, the Center is responsible for handling issues involving imported food; inspecting interstate food preparations, ie, mail, planes, and boats; securing safety and sanitation standards for supermarkets, restaurants, and other retail food establishments; as well as all food labeling issues. When the 1906 Act was adopted, food adulteration and misrepresentation were rampant. Over the years, the mandate of FDA with respect to food has expanded beyond its initial role of safeguarding food against contaminants, chemical adulteration, and disease to protecting the purchaser from economic fraud, mislabeling, excessive claims, and other nonsafety offenses such as inaccurate nutrition labeling.

FDA regulates not only the finished food product, but also the ingredients that are added to food. These ingredients may be either intentionally added to food or the unintended result of materials leaching to food from product packaging. Ingredients that are intentionally added directly to food fall into two separate categories: (*1*) pre-1958 substances and substances generally recognized as safe (GRAS) by scientific experts, and (*2*) food additives (17). There are two types of food additives, these that are added directly to food and those that are not intentionally added directly to food but come into contact with food. The latter are considered indirect food additives.

An ingredient used in food prior to January 1, 1958 can be considered GRAS under the conditions of its intended use based on common use in food. FDA prior approval generally is not necessary. A post-1958 food ingredient that is generally recognized by qualified experts as safe, under the conditions of its intended use based on scientific tests, is GRAS by definition and therefore is not a food additive and does not require FDA approval prior to use.

Any substance that is not GRAS or sanctioned by use prior to 1958 (prior sanctioned) is considered a food additive. The Act prohibits the marketing of a food additive unless FDA has published a regulation that approves the intended use of the substance (18). A food additive is deemed unsafe if it is used without an approving regulation; a food is deemed adulterated if it is, bears, or contains an unapproved food additive.

To further improve the general safety standards, the Delaney Clause was included in the Food Additives Amendment of 1958. The Delaney Clause states that no food additive or color additive can be deemed safe if it has been found to

induce cancer when ingested by humans or animals (19). The Clause acts as an absolute prohibition on the use of any additive found to cause cancer without any regard for whether, or to what extent, the substance is hazardous to human health. As scientific advances continue, both in the realm of food technology and analysis of previously undetected contaminants, the zero-risk standard of the Delaney Clause will no doubt be revisited to ensure that both the goals of safety and innovation are met.

3.5. Regulating Veterinary Products. Prior to 1968, the laws surrounding veterinary products were unclear and confusing. For example, a drug for use in feeding animals, such as a penicillin product intended to help growth and prevent diseases, was classified as both a drug and a food additive because it was added to a food for animal ingestion. The burden of seeking double clearance and preparing double paperwork before being able to market a product led to strong industry support for the New Animal Drug Amendments adopted in 1968.

Animal drug controls are similar to those for human drugs. The sponsor of a new animal drug must demonstrate both safety and effectiveness of the drug for a particular intended use before a New Animal Drug Application (NADA) is approved (20). Manufacturers of generic animal drugs may submit Abbreviated New Animal Drug Applications (ANADAs), which are comparable to abbreviated new drug applications submitted by manufacturers of human generic drugs.

A distinct concern arises in the area of veterinary drugs because of the possibility that drug residues may be conveyed to humans by the food-producing animals. Therefore, drug residues and their safety in human food remain a central issue for the Center for Veterinary Medicine (CVM). Animal drugs also include those products which promotional literature claims to improve feed efficiency and increase milk production. An animal food product is regulated under the 1968 Animal Drug Amendments if it contains a drug used in feed or premixes (21).

The food additive and GRAS rules applicable to human foods generally apply to animal food ingredients. However, the Delaney clause's prohibition against carcinogenic substances in food additives was amended to permit carcinogenic chemicals to be fed to animals if the animals are not adversely affected and no residue can be found after slaughter.

FDA's medical device regulations relating to adulteration and misbranding generally apply to devices intended for use on animals. These devices, however, are exempt from the 510(k) and PMA requirements. FDA has viewed animal grooming products as being outside of its purview.

3.6. Regulating Cosmetics. Cosmetics are among the least regulated of all FDA product categories. The Act defines a cosmetic as an article, or a component of an article, intended to be used on or in the human body for "cleansing, beautifying, promoting attractiveness, or altering the appearance" of the user (22). The FDA has no statutory preapproval authority over cosmetics. FDA's enforcement mechanism against cosmetics stems from the adulteration and misbranding sections of the Act (23). A cosmetic is considered adulterated if it contains a substance which makes it harmful to users under customary conditions of use, if it contains any "filthy, putrid, or decomposed" substance, or if it is prepared under unsanitary conditions in which the product may have become contaminated.

A cosmetic is considered misbranded if the labeling is considered false or misleading. The FDA has also challenged some cosmetics as being unapproved new drugs when the product labeling suggests therapeutic or other drug value to the consumer. For example, FDA considers cosmetic products to be drugs when these products use terms such as active ingredient or claim pharmacological effects. The FDA has stated that drug–cosmetic distinction rests upon the intended use of the product, and that the administration reviews each product on a case-by-case basis. FDA has the burden of proving that a cosmetic is unsafe. This is a significant deterrent to cosmetic regulatory action because FDA must decide the amount of risk that is acceptable.

4. Regulation of the Chemical Process Industry

The chemical process industry is highly regulated in the environmental, health, and safety area. Everything is affected, from the siting of a new facility to the transportation of raw materials and finished products, from the working conditions for employees to operating requirements for processes, packaging of finished goods, and dealings with the community. In addition to the regulatory requirements of government agencies, the chemical industry is developing standards of its own to ensure proper protection of the environment, employees, and the community. These include Responsible Care (registered by the American Chemistry Council, Formerly the Chemical Manufacturers Association); International Standard Organization (ISO) 14000; Environmental Management Systems; the sustainable development program of International Chamber of Commerce (ICC); and others.

The American Chemistry Council (ACC), the chemical industry's main trade association, developed the Responsible Care initiative in 1988. This program, which began in Canada, is a commitment on the part of the chemical industry to continuously improve health, safety, and environmental performance and to respond to public concerns. More information can be found at ACCs home page at www.americanchemisty.com. The initiative is based on 10 guiding principles and, initially, was implemented by six codes of management practices, covering Community Awareness and Emergency Response (CAER). Distribution, Employee Health and Safety, Pollution Prevention, Process Safety, and Product Stewardship. In June, 2002, ACC added a seventh code on Plant Security. More than 35 countries around the world have adopted Responsible Care and are developing their own implementation programs. Additional information can also be obtained from the Synthetic Organic Chemical Manufacturers Associations (SOCMA) at www.socma.org, which is working with ACC on Responsible Care implementation, focusing more on smaller, custom and batch chemical manufacturers.

In an attempt to bring uniformity to environmental protection, the ISO followed up the ISO 9000 series of quality standards with the ISO 14000 environmental management standards. The ISO 14001, Environmental Management Systems, is a public statement of environmental policy, which includes a commitment both to comply with relevant environmental legislation and a commitment to continual improvement; a planning process that identifies environmental

objectives at all relevant levels within the company; designated management representatives to implement the company's plans; and procedures to identify and correct nonconformance, including periodic environmental management system audits. It is expected that, similar to ISO 9000, ISO 14001 certification will also be needed by companies wishing to do business in the international market. A site with many ISO 14000 resource links is http://www.smallbiz-enviroweb.org/pollution/iso14000_links.html

The primary areas covered by EPA, and discussed below, are Water, Air, Solid and Hazardous Waste, Hazardous Chemicals, and the National Enviromental Policy Act. Under the Product Safety section, further along in this article, some other EPA laws (TSCA and FIFRA) are discussed. On-line sources for EPA laws, regulations, Federal Register citations, etc., can be found at: http://www.epa.gov/epahome/rules.html

4.1. Water. For a long time in the United States, the approach to water pollution control was through the establishment of water quality standards for receiving bodies of water, ie, rivers, streams, or lakes, with most limits established on a state-by-state basis. There was no effective, national, legal authority to limit the discharge of pollutants. In the late 1960s, the U.S. government revived an old law, the Rivers and Harbor Act of 1899 (the Refuse Act) (24). The law prohibited the discharge of anything into navigable waters unless a permit was obtained from the Corps of Engineers, thus providing a first step toward control of industrial discharges. This was followed by additional legislation, culminating in the passage of the Federal Water Pollution Control Act Amendments (FWPCA) of 1972 and the Clean Water Act (CWA) of 1977 (25). The objective of the FWPCA was to restore and maintain the chemical, physical, and biological integrity of the nation's waters.

Water Quality Standards. The first step in water quality standards is stream use classification. The individual states must decide what the uses of their water will be. The four categories, as defined by the EPA, are Class A, primary water contact recreation; Class B, propagation of desirable aquatic life; Class C, public water supplies prior to treatment; and Class D, agricultural and industrial uses. States may vary the definition of these classes to meet their own needs. The second step is to develop water-quality criteria, which is the specific concentration of a pollutant that is allowable for the designated use.

Effluent Guidelines and Standards. The CWA requires specific levels of control for dischargers. These are outlined in the Effluent Guidelines and Standards for various industrial categories. These standards limit the discharge of pollutants, usually in terms of a unit weight of pollutant per unit of either product or raw material, rather than a concentration in the discharge stream, in order to eliminate the use of dilution to meet limits.

The effluent standards are based upon the degree of reduction of a pollutant that can be achieved through the application of various levels of technology (Best Practical Technology—BPT; Best Available Technology—BAT; and Best Conventional Technology—BCT). Of special concern to the chemical industry are the following listed categories (26) (subpart N -- http://www.epa.gov/docs/epacfr40/chapt-I.info/subch-N.htm):

Part 403: general pretreatment regulations for existing and new sources of pollution
Part 411: cement manufacturing point source category
Part 413: electroplating point source category
Part 414: organic chemicals, plastics, and synthetic fibers (OCPSF)
Part 415: inorganic chemicals manufacturing point source category
Part 417: soap and detergent manufacturing point source category
Part 418: fertilizer manufacturing point source category
Part 419: petroleum refining point source category
Part 422: phosphate manufacturing point source category
Part 428: rubber manufacturing point source category
Part 439: pharmaceutical manufacturing point source category
Part 446: paint formulating point source category
Part 447: ink formulating point source category
Part 454: gum and wood chemicals manufacturing point source category
Part 455: pesticide chemicals
Part 457: explosives manufacturing point source category
Part 458: carbon black manufacturing point source category

EPA has also developed pretreatment standards for industrial facilities that discharge directly to publicly owned treatment works (POTWs), known as "indirect discharges". The three types of pollutants of principal concern are pollutants that interfere with the operation of the POTW, pollutants that contaminate the sludges produced in the POTW, and pollutants that pass through the POTW or that are otherwise incompatible. One particular concern is volatile contaminants that can be stripped into the air during conventional wastewater treatment and become air pollution problems. These pretreatment standards are included in the effluent guidelines for the different industries.

National Pollutant Discharge Elimination System Permit Program. To ensure adherence to the effluent standards, the EPA developed the National Pollutant Discharge Elimination System (NPDES) permit program. Any source discharging or planning to discharge to any U.S. water must obtain an NPDES permit. The NPDES permit application must list all pollutants to be discharged, including any priority pollutants, and it must indicate the proposed treatment methods and resultant effluent. The NPDES permit indicates the allowable discharge and requires self-monitoring. As a minimum, the effluent standards must be met, but more stringent limits may be required. Where no standards for a pollutant or industry exist, limits are decided on an individual basis.

In 1987, the Clean Water Act was amended to include storm water discharges under the NPDES permit program. EPA issued regulations in 1990 covering NPDES permit application requirements for storm water discharges associated with industrial activity. In addition to discharges generated within a facility, eg, from a process, storm water must be tested for contamination. Facilities must develop plans for minimizing storm water contact with chemicals on-site. For example, outdoor chemical storage areas should be paved and diked

to contain any storm water that could be contaminated as a result of spills. Loading and unloading areas must also be protected.

Other Laws. Many other laws have been passed to protect wetlands, coastal areas, and the oceans. The 1974 Safe Drinking Water Act (SDWA) (27) and 1996 SDWA Amendments sets maximum contaminant levels (MCLs) for a variety of chemicals that may cause any adverse effects on the health of persons and that can be present in drinking water. Although the greatest impact of this law is on providers of drinking water, there is an impact on the chemical industry. In order to protect underground sources of drinking water, the act contains a program regulating underground injection control (UIC) wells, a method used by industry for disposing of certain types of wastes. The SDWA Amendments of 1996 emphasize risk-based standard setting, monitoring relief for the public water supply systems, small water supply system flexibility, and community-empowered source water protection.

The Oil Pollution Act (OPA) of 1990 (28) streamlined and strengthened EPAs ability to prevent and respond to catastrophic oil spills. A trust fund financed by a tax on oil is available to clean up spills when the responsible party is incapable or unwilling to do so. The OPA requires oil storage facilities and vessels to develop specific plans detailing how they will respond to large discharges. Regulations for aboveground storage facilities were developed by EPA, with the Coast Guard developing regulations for oil tankers.

4.2. Air. Studies have shown that 2500 years ago lead pollution caused by Greek and Roman silver smelters was a significant problem (29). Based on analysis of lake sediments and Greenland's ice, it was found that lead contamination from smelters in southern and central Europe was carried throughout the northern hemisphere. As long ago as the thirteenth century, air pollution has been linked to the burning of coal (29). The main concern was the smell from the sulfur in the coal and the effects of the soot. It was not until many years later that the effects of air pollution on people's health were discovered.

Various laws have been passed in the United States to control air pollution. The first law that had any real effect was the Clean Air Act (CAA) of 1970, which was followed by the Clean Air Act Amendments of 1977. Most recently, the Clean Air Act Amendments (CAAA) of 1990 (30) further changed and updated the requirements. The Clean Air Act (and its amendments) is the comprehensive Federal law that regulates air emissions from area, stationary, and mobile sources. EPAs air regulations can be found at http://www.epa.gov/docs/epacfr40/chapt-I.info/subch-C.htm.

National Ambient Air Quality Standards. Under the CAA, six criterion pollutants, ie, pollutants of special concern, have been established by the EPA: sulfur oxides (SO_x), particulates, carbon monoxide (CO), nitrogen oxides (NO_x), ozone (photochemical oxidants), and lead. National Ambient Air Quality Standards (NAAQS) were developed by EPA based on threshold levels of air pollution below which no adverse effects could be experienced on human health or the environment.

The NAAQS are expressed in the form of ground level concentrations (GLC), which are the concentrations of pollutant in the ambient air as measured at ground level, in units of either micrograms per cubic meter or ppm. In order to

convert a source's emission in kilograms per hour to a GLC, dispersion modeling must be used.

State Implementation Plans. The CAA requires a state implementation plan (SIP) in each state. The SIP indicates how that state intends to meet the NAAQS. State implementation plans can include such ideas as emission limitations, economic incentives or disincentives, plant closings or relocations, and changes in either operating schedules or methods. Although many states previously required sources to obtain permits, the CAAA of 1990 established a mandatory permit program. An issue of importance to the chemical industry is the complexity of amending a permit. Industry needs to have flexibility in revising permit conditions if plant operating conditions change.

Prevention of Significant Deterioration. EPA originally issued regulations for Prevention of Significant Deterioration (PSD) in December 1974 to protect clean air areas. Three air quality classes were designated: Class I to protect pristine areas, Class II to allow moderate development, and Class III to permit more intensive development. Most areas in the United States were initially designated as Class II. Many large national parks and wildlife areas have been classified as Class I.

As part of the PSD review, the applicant must show that BACT has been applied to all sources. Items to be evaluated include energy, environmental, economic, and other costs associated with each alternative technology as well as the associated benefits of reduced emissions. Another requirement is an ambient air quality analysis to show that the new emissions do not exceed either the NAAQS or PSD increments.

Nonattainment. EPA issued final rules for the Emission Offset Policy governing development in nonattainment areas. A new source must apply the lowest achievable emission rate (LAER) for the problem pollutant and must obtain a more than equivalent offsetting emission reduction from existing sources. Either the existing sources can be owned by the same company, or the reduction can be bought from other companies. In this way, new growth is allowed while air quality improvement is achieved.

Because nonattainment areas still exist, especially in urban areas, the 1990 CAAA contain new and more stringent requirements for such areas. The ambient air quality standards for ozone are of particular concern. Controls include tighter standards on emissions from motor vehicles, use of cleaner fuels, and additional controls on industrial facilities. One of the biggest impacts on the chemical industry is more stringent requirements for minimizing the emission of volatile organic compounds (VOCs). This can include process emissions as well as emissions from storage tanks.

Emission Standards. In order to have a nationwide basis for air pollution emission controls and to set a minimum emission limit, the EPA developed New Source Performance Standards (NSPS). The NSPS set specific pollutant emission limits or describe the best available control technology (BACT) that should be applied at that source. The EPA has issued NSPS, which apply to new construction as well as to large modifications, for many different sources. Sources in the chemical industry include the following:

Sulfuric acid production units (Subpart Cb)

Industrial–commercial–institutional steam-generating units (Subpart Db)
Nitric acid plants (Subpart G)
Sulfuric acid plants (Subpart H)
Petroleum refineries (Subpart J)
Volatile organic liquid storage vessels, including petroleum liquid storage vessels (Subparts K, Ka, and Kb)
Phosphate fertilizer industry

wet process phosphoric acid plants (Subpart T)
superphosphoric acid plants (Subpart U)
diammonium phosphate plants (Subpart V)
triple superphosphate plants (Subpart W)
granular triple superphosphate storage facilities (Subpart X)
Lime manufacturing plants (Subpart HH)
Ammonium sulfate manufacture plants (Subpart PP)
Asphalt processing and asphalt roofing manufacture (Subpart UU)
Equipment leaks of VOC in the synthetic organic chemicals manufacturing industry (Subpart VV)
Bulk gasoline terminals (Subpart XX)
Rubber Tire Manufacturing Industry (Subpart BBB)
Polymer manufacturing industry (Subpart DDD)
Equipment leaks of VOC in petroleum refineries (Subpart GGG)
Synthetic fiber production facilities (Subpart HHH)
Synthetic organic chemical manufacturing industry air oxidation unit processes (Subpart III)
Synthetic organic chemical manufacturing industry distillation operations (Subpart NNN)
Petroleum refinery wastewater system VOC emissions (Subpart QQQ)

The 1990 CAAA expands the control of hazardous air pollutants (HAP). Previously, only a small number of hazardous air pollutants were regulated, under the National Emission Standards for Hazardous Air Pollutants (NESHAP). This has been expanded to cover a list of 189 pollutants, many of which are associated with chemical operations. Facilities are required to install maximum achievable control technology (MACT). The MACT standards are issued by EPA for different industries and categories of sources. The applicability of these standards is based on a facility's potential to emit and whether or not it is a major source. Some categories of MACT standards in the chemical industry are Subpart F, for National Emission Standards for Organic Hazardous Air Pollutants from the Synthetic Organic Chemical Manufacturing Industry; Subpart G, for National Emission Standards for Organic Hazardous Air Pollutants from Synthetic Organic Chemical Manufacturing Industry Process Vents, Storage Vessels, Transfer Operations, and Wastewater; Subpart H, for National Emission

Standards for Organic Hazardous Air Pollutants for Equipment Leaks; and Subpart I, for National Emission Standards for Organic Hazardous Air Pollutants for Certain Processes Subject to the Negotiated Regulation for Equipment Leaks.

Accidental Release Provisions. The 1990 CAAA includes provisions similar to OSHAs process safety management standard for minimizing the accidental release of air toxics. Based on types and quantities of hazardous chemicals on-site, a facility is required to develop and implement risk management plans. The plans must be designed to prevent, detect, and respond to accidental hazardous chemical releases. In addition, facilities must provide this information to their local communities. The phrase that has been used to describe this information is worst-case scenarios. These requirements were revised under the Chemical Safety Information, Site Security and Fuels Regulatory Relief Act, enacted in 1999 (31).

4.3. Solid and Hazardous Waste. Regulation of pollution resulting from solid waste disposal was formulated at a much slower pace than regulation of air or water pollution. It was not until the Resource Conservation and Recovery Act (RCRA) of 1976 (32) was passed that substantial controls were authorized. RCRA gives EPA control of hazardous waste from "cradle-to-grave". In 1984, HSWA, the Federal Hazardous and Solid Waste Amendments were enacted. Other related laws are the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA), commonly known as Superfund, in 1980, and the Superfund Amendments and Reauthorization Act (SARA) in 1986. These additional laws are discussed below. EPA has information about RCRA on-line at: http://www.epa.gov/rcraonline/.

The main objectives of RCRA are to protect public health and the environment and to conserve natural resources. The act requires EPA to develop and administer the following programs: solid waste disposal practices providing acceptable protection levels for public health and the environment; transportation, storage, treatment, and disposal of hazardous wastes practices that eliminate or minimize hazards to human health and the environment; the use of resource conservation and recovery whenever technically and economically feasible; and federal, state, and local programs to achieve these objectives.

The section of the RCRA of most concern to the chemical industry is Subtitle C, the hazardous waste management regulations. The purpose of this section is to regulate hazardous wastes from their generation to their disposal. Facilities that generate, treat, store, or dispose of hazardous wastes are covered by these regulations.

The RCRA definition of solid waste covers a wide range of materials, including solid, liquid, semisolid, or contained gaseous material resulting from industrial, commercial, mining, and agricultural operations. A hazardous waste is a substance that must either be listed by the EPA or have a hazardous characteristic. Several types of solid wastes are specifically excluded from hazardous waste regulation because of their great volume or for other reasons. These include household wastes and some agricultural, mining, and fossil fuel combustion and exploration wastes.

A solid waste is considered hazardous if it is either a listed waste or a characteristic waste. Listed wastes include a list of specific processes that generate a

waste and a list of discarded commercial chemical products. There are four hazardous waste characteristics: ignitability, corrosivity, reactivity, and toxicity. The last refers to the leachability of a waste and the resultant toxicity in the groundwater using the analytical method referred to as toxicity characteristic leaching procedure (TCLP). A list of substances included under TCLP is shown in Table 2 (Section 261.24, http://www.access.gpo.gov/nara/cfr/cfrhtml_00/Title_40/40cfr261_00.html)

It is the generator's responsibility to determine if a substance is hazardous. Generator requirements include recordkeeping, labeling, using proper containers, providing information to transporters, following the manifest system, and periodic reporting to the EPA. The manifest system is a set of papers that is passed from the generator to the transporters of the waste, to those responsible for final disposal, and back to the generator to signify that the waste has been disposed of properly.

Regulations for owners and operators of hazardous waste treatment and storage and disposal facilities (TSDFs) cover both interim and general status. Any facility operating prior to November 30, 1980, is considered existing and is granted interim status if notification has been sent to EPA. The requirements cover operating methods and location, design, and construction of TSDFs. These include tanks; surface impoundments; waste piles; land treatment; landfills; incinerators; thermal treatment; chemical, biological, and physical treatment; and underground injection.

Groundwater and air quality monitoring are required for all facilities that have the potential to generate emissions. There are also requirements for contingency plans in the case of accidents, closure and post-closure plans, and financial requirements to ensure that closure plans can be followed. Permit applications must include an estimate of the composition, quantity, concentration, and frequency or rate of disposal, treatment, transport, or storage.

Regulations covering nonhazardous solid waste are mainly at the state and local level. Some states are starting to run out of space for landfills. As a result, regulations are starting to increase for nonhazardous solid waste. Most of these are designed to encourage better management of solid waste, including source reduction, recycling, and reuse. One type of solid waste that is regulated separately is medical waste. Although this typically comes from hospitals and doctors' offices, some laboratory wastes from chemical plants, such as syringes used to inject samples into analytical equipment, may need to be handled specially.

RCRA also regulates underground storage tanks (USTs). The USTs must be registered with a facility's designated state agency. Regulations include requirements for leak detection or inventory control system and tank testing; recordkeeping and reporting; corrective action; financial responsibility for corrective action and/or third-party liability; and closure once the tanks are taken out of use.

Under HSWA, waste minimization and a national land disposal ban program were promulgated. Included under HSWA are these requirements: proper hazardous waste management; waste minimization; reduction in land disposal practices; prohibition of open dumping; encouragement of state authriozed RCRA programs; encouragement of research and development; and encouragement of recovery, recycling, and treatment alternatives.

In 1980, the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA), known as the Superfund legislation (33) was authorized. This act provides a means for the federal government to collect money from industry for use in cleaning existing and abandoned hazardous waste disposal sites and spills. Two kinds of response actions are allowed: short-term removals where prompt response is needed to control releases or threatened releases, particularly those that are life threatening and long-term remedial response actions to permanently reduce the dangers associated with releases of hazardous substances posing a serious threat. For operating facilities, there are regulations requiring reporting of spills and releases, based on reportable quantities (RQs), to the National Response Center (NRC). In addition, requirements for cleanup of facilities contaminated by past releases, as well as abandoned contaminated facilities, are included.

CERCLA was amended in 1986 by the Superfund Amendments and Reauthorization Act (SARA) (34). Several important changes were made including: stressed the importance of permanent remedies and innovative treatment technologies in cleaning up hazardous waste sites; required Superfund actions to consider the standards and requirements found in other State and Federal environmental laws and regulations; provided new enforcement authorities and settlement tools; increased State involvement in every phase of the Superfund program; increased focus on human health problems posed by hazardous waste sites; encouraged greater citizen participation in making decisions on how sites should be cleaned up; and increased the size of the trust fund to $8.5 billion.

In 1990, the Pollution Prevention Act (PPA) (35) was authorized. The purpose is to look at source reduction rather than waste treatment and disposal. PPA focuses industry, government, and public attention on reducing the amount of pollution through cost-effective changes in production, operation, and raw materials use. Other areas of pollution prevention looked at includes other practices that increase efficiency in the use of energy, water, or other natural resources. Such practices include recycling, source reduction, and sustainable agriculture.

4.4. Hazardous Chemicals. The Emergency Planning and Community Right-to-Know Act (EPCRA) (36), promulgated as part of the Superfund Reauthorization Act and originally known as SARA, Title III, requires facility emergency plans, spill and release reporting, annual inventory reporting, and annual toxic chemical emissions and pollution prevention reporting. It is known as the national legislation on community safety. The regulations under SARA and EPCRA can be found at http://www.epa.gov/docs/epacfr40/chapt-I.info/subch-J.htm.

The annual toxic emissions reports are called Toxic Release Inventory (TRI) reports, also known as Section 313 or Form R reports. These reports must include information on any on- or off-site releases, disposal, treatment, or recycling of the listed toxic chemicals. Reporting requirements depend on the amount of the chemicals used or manufactured as well as the type of use. Sections 311 and 312 cover right-to-know requirements.

The facility emergency plans and the annual inventory reporting must be shared with the community, through the local emergency planning committee

(LEPC) and the state emergency response commission (SERC). The facility must also provide material safety data sheets (MSDSs) to the LEPC and other emergency responders. Because the SERCs and LEPCs include fire fighters, health officials, government representatives, the media, community groups, industrial facilities, and emergency managers, all necessary elements of the planning process should be represented.

Both CERCLA and EPCRA have requirements for reporting releases to the air, ground, or water. Lists of reportable chemicals or family of chemicals and their reportable quantity (RQ) have been issued (37). A reportable quantity is the amount, in pounds or kilograms, below which a release does not have to be reported. CERCLA requires only the reporting of releases from the CERCLA list; however, EPCRA requires reporting releases of both EPCRA- and CERCLA-listed substances. Reportable releases under CERCLA must be reported to the National Response Center, at (800) 424–8802. Reporting under EPCRA requires notifying the facility's LEPC (or relevant local emergency response personnel if there is no LEPC) and the SERC of any state likely to be affected. If a facility is near the border of another state, that state may have to be notified as well. Notification is required to be immediate, which is usually defined as within 30 min of the release. State or local authorities may have additional or different reporting requirements. Failure to report release in a timely manner can result in severe penalties from the regulatory authorities.

4.5. Multimedia Permitting. EPA has started looking at chemical plants with a multimedia view, ie, not just an air problem or a water problem, but how all aspects of a plant's operations, emissions, releases, etc, fit together. The driving force behind this is pollution prevention, not just treating wastes that are produced, but eliminating the production of the wastes in the first place. Of concern to the chemical industry is the possibility of toxic use reduction (TUR) regulations. These require reduction in use, or even elimination, of chemicals that are deemed toxic. The chemical industry believes that with sufficient knowledge and proper controls, chemicals can be handled safely. Their focus is on reuse and recycling of chemicals in order to minimize emissions and releases.

4.6. National Environmental Policy Act. The principal goal of the National Environmental Policy Act (NEPA) (38) is to establish a national policy that ensures continued growth and technological advancement while maintaining the quality of the environment. It is considered the basic national charter for protection of the environment. It establishes policy, sets goals, and provides means for carrying out the policy.

Any Federal agency sponsoring action that significantly affects the environment, eg, granting a construction permit or introducing new legislation, must issue a detailed report describing the environmental impact of the proposed action and alternatives. This report is called an environmental impact statement (EIS). An EIS is written and issued by the federal agency involved with a particular project. The agency, however, relies on the owners of the proposed facility to provide the information contained in the EIS. The section on alternatives is considered the most important part of the EIS. The proposed project and its alternatives are usually described in detail. The environmental impacts of the proposal and the alternatives are presented. Based on all of this

information, the federal agency determines if the proposed project is environmentally acceptable.

5. Health and Safety Factors

5.1. Product Safety. *Toxic Substances Control Act.* EPA regulates the manufacture, use, and exposure to hazardous or toxic chemicals under a number of laws. For the chemical industry, the law of prime concern is the Toxic Substance Control Act (TSCA) (39), which was passed by the U.S. Congress in 1976. The two main goals of TSCA are acquisition of sufficient information to identify and evaluate potential hazards from chemical substances, and regulation of the production, use, distribution, and disposal of these substances. TSCA regulations can be found at http://www.epa.gov/docs/epacfr40/chapt-I.info/subch-R.htm.

One important aspect of TSCA is the premarket or import notification program. Before a manufacturer produces or imports a new chemical substance, EPA must be given 90 days' notice, the premanufacture notification (PMN). The notice includes all testing done by the manufacturer to determine the health effects of the chemical. Information on a facility's pollution prevention plans with regard to the manufacturing operation must also be included. EPA then has 45 days from the end of the review period to determine if the production or distribution of the chemical should be restricted or prohibited because the chemical presents an unreasonable risk. The manufacturer has an additional 30 days to object to EPAs decision. EPA has established an inventory of chemicals manufactured or processed in the United States (40). Any substance not on the list by August 30, 1980 is considered a new chemical and must be described in the premarket notification. Exemptions are given for substances registered as pesticides or regulated by the FDA.

As part of TSCA, EPA can require the testing of any chemical if there is the possibility of an unreasonable risk to health or environment or if there is significant human or environmental exposure. If the substance poses an unreasonable risk, EPA can prohibit the manufacture, processing, or distribution of the substance; limit the amount of the substance that can be manufactured, processed, or distributed; prohibit a particular use for the substance; limit the concentration of the substance during manufacture, processing, or distribution; regulate disposal methods for the substance; and require manufacturers to maintain records of the process and to conduct tests to assure compliance with EPA rules.

Another section of TSCA requires the manufacturer to notify EPA if there is any indication of substantial risk from any chemical. Failure to do so by the manufacturer within a specified time period may result in civil penalties or possibly criminal prosecution.

TSCA also addresses the problem of polychlorinated biphenyls (PCBs) and chlorinated fluorocarbons (CFCs). EPA has developed regulations on the cleanup, handling, and disposal of PCBs. The manufacture and use of CFCs has been banned for all but essential uses, in accordance with the Montreal Agreement, an international treaty on worldwide use of CFCs.

Federal Insecticide, Fungicide, and Rodenticide Act. The Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) (41) covers the use and manufacture of pesticides, rodenticides, etc, and includes such things as biocides and preservatives. Prior to manufacture, these regulated products must be registered with EPA. Registration assures that pesticides will be properly labeled and will not cause unreasonable harm to the environment. There are very specific labeling and container requirements for these products. Users (farmers, utility companies, and others) must register when purchasing pesticides. Later amendments to the law require users to take exams for certifications as applicators of pesticides. More details on these regulatory requirements are given in the articles Fungicides, Pesticides, Insect control technology, and Industrial antimicrobial agents. Regulations under FIFRA can be found at http://www.epa.gov/docs/epacfr40/chapt-I.info/subch-E.htm.

Food, Drug, and Cosmetic Protection. There are several laws (with corresponding regualtions) that protect food, drugs, and cosmetics. The first is the Federal Food, Drug, and Cosmetic Act (FFDCA) (42). The other one of interest to the chemical industry is Food Quality Protection Act (FQPA) (43).

Transportation. The U.S. Department of Transportation (www.dot.gov/) regulates the transport, packaging, and handling of hazardous substances, including chemicals. In addition, there are international laws and regulations. Substances are characterized based on their type of hazard and assigned identification numbers. The type of packaging that can be used for different types of hazards is regulated. For example, there are only certain types of containers that can be used for flammables or corrosives. When hazardous materials are transported, the vehicle, eg, truck, tank truck, and tank car, must be placarded to show the hazard. The bill of lading must describe the material, including the hazards. The material safety data sheet (MSDS) must be available. In addition, there are many training requirements for those employees handling, packaging, or transporting hazardous chemicals. Only certified transporters may transport hazardous chemicals.

5.2. Employee Safety. *Occupational Safety and Health Act.* OSHA has broad responsibilities for protecting the workplace. The Occupational Safety and Health Act is administered by the Occupational Safety and Health Administration under the U.S. Department of Labor (44). The act covers all health and safety aspects of a worker's environment. OSHA laws, regulations, *Federal Register* citations, etc., can be found on-line at: http://www.osha.gov/fso/ca.html.

Subpart Z of the Act, Toxic and Hazardous Substances, lists allowable employee exposure to many different chemical substances (45). These are given as ambient air concentrations over a certain time period, usually an 8-h time-weighted average. Sometimes a ceiling concentration is given as well. Certain substances, eg, vinyl chloride, benzene, and formaldehyde, are discussed in terms of necessary controls and limits. The monitoring of employee exposure is called industrial hygiene (qv).

In the Hazard Communication Standard, OSHA requires that all employees are trained in the hazards of the materials they are working with. This standard also requires that MSDSs be available for all hazardous chemicals at the worksite, accompany all shipments, and be sent to all customers. An MSDS summarizes all of the important health, safety, and environmental information

about a substance. A version of this standard also applies to laboratories, including research and development facilities, and requires the development of a laboratory hygiene plan.

Included in the OSHA regulations are standards for safe work practices such as lock-out/tag-out and confined space entry, personal protective equipment, storage of hazardous materials, welding process, forklift operation, and requirements for fire protection. Basically, all activities within a chemical facility are covered by OSHA standards.

In response to a number of major incidents at chemical facilities, OSHA has issued process safety management standards. For a selected list of hazardous substances, a facility is required to have a process safety management program in place. This includes training to ensure employees know how to deal with hazards, analyses of processes using these hazardous substances, and management of change to ensure that any changes to equipment, processes, types of chemicals used, etc, are analyzed. Unlike EPAs accidental release provisions that focus on protection of the community, the focus of this standard is on protecting employees on-site.

After debating the issue for over 20 years, on April 5, 2002, OSHA finally announced its Comprehensive Plan on Ergonomics to address musculoskelatal disorders (MSDs) in the workplace. OSHA is using a four-pronged approach to reduce injuries and illnesses from MSDs in the workplace. These include: guidelines, enforcement, outreach and assistance, and research. OSHA will develop industry or task-specific guidelines for a number of industries based on current incident rates and available information about effective and feasible solutions. This work will take into account guidelines and best practices already developed including OSHAs own Meatpacking Guidelines.

The National Institute of Occupational Safety and Health (NIOSH), under the Department of Health and Human Services, works with OSHA. It is NIOSHs responsibility to determine safe exposure limits for chemical substances and to recommend to OSHA that these limits be adopted as standards.

6. Acronyms. Acronyms in common use in the regulatory arena include the following [a listing of environmental terms and acronyms from EPA can be found on-line at http://www.epa.gov/OCEPAterms/]:

Air quality control region (AQCR)
Advanced wastewater treatment (AWT)
Best available control technology (BACT)
Best available technology (BAT)
Best conventional pollutant control technology (BCT)
Biochemical oxygen demand (BOD)
Best practicable control technology (BPCT)
Clean Air Act (CAA)
Clean Air Act Amendments (CAAA)

Community Awareness and Emergency Response, under Responsible Care (CAER)
Comprehensive Assessment Information Rule, under TSCA (CAIR)
Confidential business information (CBI)
Comprehensive Environmental Response, Compensation, and Liability Act, also known as the Superfund Law (CERCLA)
Chlorinated fluorocarbon (CFC)
Code of Federal Regulations (CFR)
Chemical oxygen demand (COD)
Consumer Product Safety Commission (CPSC)
Clean Water Act (CWA)
Department of Transportation (DOT)
Environmental impact statement (EIS)
Environmental Protection Agency (EPA)
Environmental Planning and Community Right-to-Know Act (EPCRA)
Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA)
Freedom of Information Act (FOIA)
Federal Water Pollution Control Act (FWPCA)
Good engineering practice (GEP)
Ground-level concentration (GLC)
Good laboratory practice (GLP)
Government Printing Office (GPO)
Hazardous air pollutant (HAP)
Lowest achievable emission rate (LAER)
Local Emergency Planning Committee (LEPC)
Leaking underground storage tanks (LUST)
Maximum achievable control technology (MACT)
Material Safety Data Sheet (MSDS)
National Ambient Air Quality Standard (NAAQS)
National Environmental Policy Act (NEPA)
National Emission Standards for Hazardous Air Pollutants (NESHAP)
National Institute for Occupational Safety and Health (NIOSH)
Nitrogen oxides (NOx)
National Pollutant Discharge Elimination System (NPDES)
Notice of Proposed Rulemaking (NPRM)
National Response Center or Nuclear Regulatory Commission (NRC)
New Source Performance Standard (NSPS)
Occupational Safety and Health Act (and Administration) (OSHA)
Polychlorinated biphenyl (PCB)
Permissible exposure limit (PEL)
Premanufacture notification, under TSCA (PMN)

Publicly owned treatment work (municipal wastewater treatment facility) (POTW)
Potentially responsible party, under Superfund (PRP)
Prevention of Significant Deterioration (PSD)
Resource Conservation and Recovery Act (RCRA)
Reportable quantity (RQ)
Superfund Amendments and Reauthorization Act (SARA)
Safe Drinking Water Act (SDWA)
State Emergency Response Commission (SERC)
Standard Industrial Classification Code (SIC)
State implementation plan (SIP)
Sulfur oxides (SOx)
Significant new use rule, under TSCA (SNUR)
Synthetic organic chemical industry (SOCMI)
Spill prevention control and countermeasure plan (SPCC Plan)
Toxicity characteristic leaching procedure (TCLP)
Threshold planning quantity (TPQ)
Toxic Release Inventory (TRI)
Toxic Substances Control Act (TSCA)
Treatment, storage, and disposal facility (TSDF)
Total suspended particulates (air) (TSP)
Total suspended solids (wastewater) (TSS)
Time-weighted average (TWA)
Underground-injection controls (UIC)
Underground storage tank (UST)
Volatile organic compounds (VOC)

BIBLIOGRAPHY

"Regulatory Agencies" in *ECT* 3rd ed., Vol. 20, pp. 108–127, by N. R. Passow, C-E Lummus. "Regulatory Agencies: in *ECT* 4th ed., Vol. 21, pp. 149–168, by N. R. Passow, Lonza, Inc.; G. L. Yingling and S. Onel, McKenna & Cuneo, LLP. "Regulatory Agencies, Survey" in *ECT* (online), posting date: December 4, 2000, by Nancy R. Passow, Lonza, Inc.

CITED PUBLICATIONS

1. The official 2002 US NAICS Manual North American Industry Classification System–United States, 2002 includes definitions for each industry, tables showing correspondence between 2000 NAICS and 1997 NAICS, and a comprehensive index. A 2002 CD-ROM is available. See the NTIS web site lists the 2002 Manual.

2. W. Schultz, testimony before the Subcommittee on Health and the Environment of the House Committee on Commerce, 104th Congress, 1st session, Washington, D.C., Feb. 2, 1995. Federal Food, Drug, and Cosmetic Act of 1938 (as amended), 21 USC §§ 321–395 1995).
3. 21 CFR §§1–1499 (April 2005).
4. Ref. 2, §321(p), 355; Ref. 3, part 310.
5. Ref. 3, part 312.
6. Ref. 3, part 314.
7. Ref. 3, part 211.
8. Ref. 3, parts 330–369.
9. Ref. 2, §355(j).
10. Ref. 2, §§356–357.
11. Ref. 3, part 601.
12. Ref. 2, §306(c).
13. Ref. 2, §360(k); Ref. 3, part 807.
14. Ref. 2, §360(e); Ref. 3, part 814.
15. Ref. 3, part 812.
16. Ref. 3, part 820.
17. Ref. 2, §321(s); Ref. 3, part 170.
18. Ref. 2, §348(a).
19. Ref. 2, §348(c)(3).
20. Ref. 2, §§321(w) and 360(b); Ref. 3, parts 510 and 514.
21. Ref. 2, §321(x), 360(b).
22. Ref. 2, §321(i).
23. Ref. 2, §§361–362.
24. *The Rivers and Harbor Act of 1899*, 33 USC §§401–413, and Executive Order 11574.
25. *Clean Water Act of 1977*, 33 USC §§1251 et seq.
26. *Effluent Guidelines and Standards*, 40 CFR Chapter 1, subchapter N, Parts 400–471.
27. *Safe Drinking Water Act*, 42 USC §§300f et seq. (1974).
28. *The Oil Pollution Act of 1990*, 33 USC 2702 to 2761.
29. "Ancient Silver Smelters Polluted the Hemisphere", *The Record*, Sept. 23, 1994, p. A-23; and P. Brimblecombe, "Attitudes and Responses Towards Air Pollution in Medieval England," *Air Poll. Contr. Assoc.* (Oct. 1976).
30. *Clean Air Act*, 42 USC §7401, et seq. (1970).
31. *Chemical Safety Information, Site Security & Fuels Regulatory Relief Act*, 42 USC 7412(r) (1999).
32. *Resource Conservation and Recovery Act* of 1976, 42 USC §§321 et seq.
33. *Comprehensive Environmental Response, Compensation, and Liability Act*, 42 USC §§9601 et seq.
34. *Superfund Amendment and Reauthorization Act*, 42 USC 9601 et seq. (1986).
35. *Pollution Prevention Act*, 42 USC 13101 and 13102 et seq. (1990).
36. *Emergency Planning and Community Right-to-Know Act*, 42 USC §§11001 et seq.
37. *Comprehensive Environmental Response, Compensation, and Liability Act* (CERCLA) Reportable Releases: 40 CFR 302, "EPA Designation, Reportable Quantities, and Notification Requirements for Hazardous Substances under CERCLA," Table 302.4, "Lists of Hazardous Substances and Reportable Quantities;" EPCRA Section 304 Reportable Releases: 40 CFR 355, "The List of Extremely Hazardous Substances and their Threshold Planning Quantities," Appendix A, Alphabetical Order, and Appendix B, CAS Number Order.
38. *National Environmental Policy Act*, 42 USC §§4321–4347.

39. *Toxic Substances Control Act*, 15 USC §§2601 et seq. (1976).
40. *Toxic Substances Control Act*, Chemical Substances Inventory; further information can be obtained from Industry Assistance Office, Pesticides and Toxic Substances, Environmental Protection Agency, Washington, D.C.
41. *Federal Insecticide, Fungicide and Rodenticide Act*, 7 USC 135 et seq. (1972).
42. *Federal Food, Drug, and Cosmetic Act*, 21 USC 301 et seq.
43. *Food Quality Protection Act*, Public Law 104-170 (1996).
44. *Occupational Safety and Health Act*, 29 USC §§651–678.
45. *Occupational Safety and Health Act*, 29 CFR 1910.1000.

GENERAL REFERENCES

Subscriptions to *Federal Register* can be obtained through the Superintendent of Documents, U.S. Government Printing Office, Washington, D.C., 20402, (202) 512–1800. *Federal Register* and the *Codes of Federal Regulations* are available at those public libraries designated as U.S. Federal repositories; The US Government Printing Office can be accessed on-line at: http://www.access.gpo.gov/. Their on-line bookstore is at http://bookstore.gpo.gov. On-line find the Federal Register at http://www.gpo.gov/su_docs/aces/aces140.html

D. O. Beers, *Generic and Innovator Drugs: A Guide to FDA Approval Requirements*, th ed., Aspen Law and Business/Aspen, Engelwood Cliffs, N.J., 1995.

Food and Drug Administration, Center for Devices and Radiological Health, *An Introduction to Medical Device Regulations*, HHS Publication No. 92-4222, U.S. Department of Health and Human Services, Public Health Service, Rockville, Md., 1992.

Food and Drug Administration, History Office, *A Guide to the Resources on the History of the Food and Drug Administration*, GPO, Washington, D.C., 1995.

J. E. Foulke, *Cosmetic Ingredients*, HHS Publication No. 93-5013, Department of Health and Human Services, GPO, Washington, D.C., 1993.

Decoding the Cosmetic Label, HHS Publication No. 95-5016, Department of Health and Human Services, GPO, Washington, D.C., 1995.

W. F. Janssen, *The U.S. Food and Drug Law: How It Came, How It Works*, HHS Publication No. 92-1054, Department of Health and Human Services, GPO, Washington, D.C., 1992.

J. T. O'Reilly, *Food and Drug Administration*, 2 vols, 2nd ed., Shepard's/McGraw-Hill, Colorado Springs, Colo., 1993.

D. Stehlin, *Cosmetic Safety More Complex Than At First Blush*, HHS Publication No. 93-5012, Department of Health and Human Services, GPO, Washington, D.C., 1993.

BOOKS

Environmental Management Source Book, 1994–1995, Environment Today, Enterprise Communications Inc., Marietta, Ga.; annual issue as part of monthly magazine subscription.

R. L. Hoover and co-workers, *Health, Safety, and Environmental Control*, Van Nostrand Reinhold Co., Inc., New York, 1989.

R. J. Lewis, ed., *Sax's Dangerous Properties of Industrial Materials*, 11th ed., John Wiley & Sons, Hoboken, N.J., 2004.

T. Wagner, *The Complete Handbook of Hazardous Waste Regulation*, Perry-Wagner Publishing Co., Inc., 1988.

TRADE ASSOCIATIONS AND OTHER SOURCES OF INFORMATION

American Chemistry Council (formerly the Chemical Manufacturers Association), 1300 Wilson Blvd., Arlington, Va., 22209, (703) 741–5000, which offers information about Responsible Care (a registered trademark of ACC) and regulatory impact on the chemical industry, www.americanchemistry.com

Synthetic Organic Chemical Manufacturers Association, 1850 M St. NW, Suite 700, Washington, D.C., 20036, (202) 721–4100, which offers information about regulatory impact on the chemical industry, particularly small and batch operations, www.socma.org

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Table 1. **Federal Agencies and Their Functions**

Agency	Alias	Function
Agriculture Department	USDA	agriculture, animal and plant health inspection, forest service, food safety, Rural Electrification Administration, soil conservation service
Commerce Department	Commerce	Census Bureau, economics, trade, National Oceanic and Atmospheric Administration, Patent and Trademark Office
Department of Defense	DOD	Engineers Corps, dredge and fill operations, waterways, etc
Energy Department	DOE	all aspects of energy use, conservation, costs, etc
Health and Human Services Department	HHS	Food and Drug Administration, National Institute for Occupational Safety and Health (NIOSH)
Interior Department	Interior	land management, fish and wildlife, Geological Survey, mines, surface mining and reclamation
Justice Department	Justice	Antitrust Division, enforcement activities
Labor Department	Labor	employment standards and statistics, OSHA, Mine Safety and Health Administration (MSHA)
Transportation Department	DOT	Coast Guard; Federal Aviation Administration (FAA); highway, railroad, and maritime administration; hazardous material shipping
Treasury Department	Treasury	Alcohol, Tobacco, and Firearms Bureau (ATF), Customs Service, Internal Revenue Service
Council on Environmental Quality	CEQ	provides policy advice on environmental matters; implements National Environmental Policy Act (NEPA); coordinates environmental concerns among other agencies
Nuclear Regulatory Commission	NRC	ensures that radioactive materials are used and nuclear facilities are operated with regard for environment and public health, safety, and security
Office of Management and Budget	OMB	reviews regulations to ensure that they are cost-effective; approves paperwork or other information-gathering requirements

Table 2. **Maximum Concentration of Contaminants for Toxicity Characteristic**

EPA hazardous waste number	Contaminant	CAS Registry Number	Regulatory level, mg/L
D004	arsenic	[7440-38-2]	5.0
D005	barium	[7440-39-3]	100.0
D018	benzene	[71-43-2]	0.5
D006	cadmium	[7440-43-9]	1.0
D019	carbon tetrachloride	[56-23-5]	0.5
D020	chlordane	[57-74-9]	0.03
D021	chlorobenzene	[108-90-7]	100.0
D022	chloroform	[67-66-3]	6.0
D007	chromium	[7440-47-3]	5.0
D023	*o*-cresol	[95-48-7]	4200.0
D024	*m*-cresol	[108-39-4]	4200.0
D025	*p*-cresol	[106-44-5]	4200.0
D026	cresol	[1319-77-3]	4200.0
D016	2,4-dichlorophenoxy	[94-75-7]	10.0
D027	1,4-dichlorobenzene	[106-46-7]	7.5
D028	1,2-dichloroethane	[107-06-2]	0.5
D029	1,1-dichloroethylene	[75-35-4]	0.7
D030	2,4-dinitrotoluene	[121-14-2]	30.13
D012	endrin	[72-20-8]	0.02
D031	heptachlor (and its epoxide)	[76-44-8]	0.008
D032	hexachlorobenzene	[118-74-1]	30.13
D033	hexachlorobutadiene	[87-68-3]	0.5
D034	hexachloroethane	[67-72-1]	3.0
D008	lead	[7439-92-1]	5.0
D013	lindane	[58-89-9]	0.4
D009	mercury	[7439-97-6]	0.2
D014	methoxychlor	[72-43-5]	10.0
D035	methyl ethyl ketone	[78-93-3]	200.0
D036	nitrobenzene	[98-95-3]	2.0
D037	pentachlorophenol	[87-86-5]	100.0
D038	pyridine	[110-86-1]	35.0
D010	selenium	[7782-49-2]	1.0
D011	silver	[7440-22-4]	5.0
D039	tetrachloroethylene	[127-18-4]	0.7
D015	toxaphene	[8001-35-2]	0.5
D040	trichloroethylene	[79-01-6]	0.5
D041	2,4,5-trichlorophenol	[95-95-4]	400.0
D042	2,4,6-trichlorophenol	[88-06-2]	2.0
D017	2,4,5-trichlorophenoxy (silvex)	[93-72-1]	1.0
D043	vinyl chloride	[75-01-4]	0.2