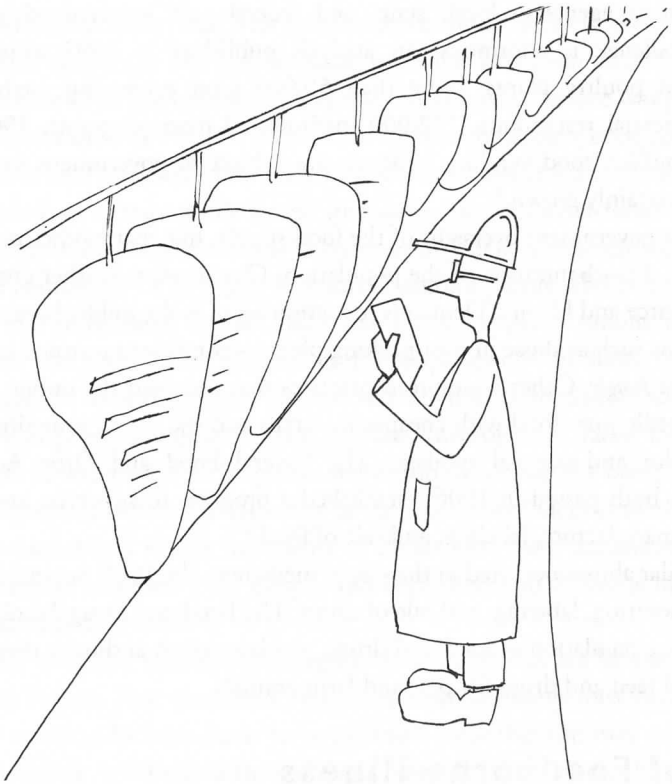
CHAPTER

23

Safe Food and Drugs: An Ongoing Regulatory Battle



Meat Inspection

Americans are very concerned about the safety of their food. Although Americans used to think of their food supply as the safest in the world, this confidence has been shaken in the last few years by widely publicized outbreaks of illnesses caused by foods ranging from bagged spinach to peanut butter.

Since only the most serious cases of foodborne disease are reported, the extent of the problem is unclear. The Centers for Disease Control and Prevention (CDC) has estimated that 76 million people contract foodborne diseases each year, with 5000 deaths, an estimate that has not changed in years.[1] With some 300 million people eating three meals per day, not counting snacks, however, the likelihood of getting sick from eating a single meal is extremely small. Many government agencies—local, state, and federal—are involved with regulating food safety. The challenge is enormous: an analysis published in 1992 estimated that some 6100 meat and poultry plants, more than 50,000 food processing establishments, about 537,000 commercial restaurants, 172,000 institutional food programs, 190,000 retail food stores, and 1 million food vending locations are subject to government inspection, and the numbers have certainly grown.[2]

The need for government oversight of the food supply, like many other public health measures, arose with the urbanization of the population. City dwellers neither grew their own food nor knew its source and history. Demands for action arose as the public became aware of unhygienic conditions such as those in meatpacking plants—conditions revealed in Upton Sinclair's 1906 novel, *The Jungle*. Other widespread practices that outraged the public included adulteration of supposedly pure food with cheaper materials and the use of sometimes toxic additives to improve color and conceal spoilage. The Federal Food and Drug Act and the Meat Inspection Act, both passed in 1906, established a program to supervise and control the circumstances of manufacture, labeling, and sale of food.[3]

Because similar abuses occurred in the sale of medicines, the 1906 Act included provisions to control manufacturing, labeling, and sale of drugs. The Food and Drug Administration (FDA), created to oversee regulation of food and drugs, was later given authority over cosmetics, medical devices, and feed and drugs for pets and farm animals.

Causes of Foodborne Illness

Foodborne diseases are most often caused by contamination of foods with bacteria, viruses, or parasites due to breakdowns in sanitation and/or proper food handling practices. *Salmonella* bacteria, for example, are common contaminants of poultry, meat, and eggs. Infected hens may transfer the pathogens to the eggs as they are being formed in the ovary. Although the bacteria are killed when the food is thoroughly cooked, people who prefer their meat rare or their egg

yolks runny are at risk of salmonellosis, especially if the food has been kept at room temperature long enough for the bacteria to flourish. Caesar salad dressing made with raw eggs and homemade eggnog are particularly risky. The symptoms of salmonellosis, like symptoms of most types of food poisoning, include vomiting, diarrhea, and abdominal pain.

Like *Salmonella* in poultry and eggs, *Escherichia coli* 0157:H7 is widespread in beef, probably due to the way livestock are raised and processed. To prevent illness and deaths such as those that occurred in 1993 in Seattle (described in Chapter 10), hamburgers must be cooked more thoroughly than the previous standard required. In addition to its occurrence in ground beef, *E. coli* 0157:H7 has also turned up in other foods, including salami, raw milk, lettuce, alfalfa sprouts, and unpasteurized apple juice. The bacteria are common in the intestinal tracts of cows and are excreted with their feces. The contaminated juice may have been made from apples that fell onto ground where cows had wandered, and the contaminated lettuce was prepared under unsanitary conditions near a cow pen.[4,5] The alfalfa sprouts could have been contaminated by being grown in fields near cattle feed lots and irrigated with water contaminated by manure.[6]

In fact, fresh produce is responsible for an increasing proportion of foodborne illness. In 2006, fruits and vegetables caused almost as many cases of illness as were caused by beef, poultry, fish, and eggs combined.[7] A hepatitis A outbreak among people who had eaten at a Chi-Chi's restaurant in Pennsylvania in fall 2003 was traced to green onions imported from Mexico. More than 600 people were infected, and 3 people died.[8,9] In 2008, the largest foodborne disease outbreak in the previous decade was attributed to *Salmonella*-contaminated jalapeño and serrano peppers imported from Mexico. Investigators traced infection to two farms, where a pool of water used for irrigation was found to contain the bacteria. The investigation was made especially difficult because few of the interviewed victims recalled eating peppers, which were probably a minor ingredient in dishes that were remembered to contain tomatoes. The outbreak sickened 1442 people and contributed to 2 deaths in 43 states, the District of Columbia, and Canada.[10]

Fish and shellfish are likely to harbor pathogenic microbes if they are harvested from waters polluted by human sewage. Raw clams and oysters are especially dangerous: because they grow in shallow coastal waters, which are likely to be polluted, these shellfish may carry cholera and related bacteria, hepatitis A virus, and the common Norwalk virus, all capable of causing disease in humans. Fish used uncooked for Japanese dishes such as sushi and sashimi and South American ceviche may also carry parasites harmful to humans.[3]

Some bacteria cause illness by way of toxins they produce rather than by simple infection. Thus these contaminants are hazardous even after the food is cooked. The best-known—and deadliest—of these are the bacteria that cause botulism. They flourish in the absence of oxygen and are most commonly associated with home-canned vegetables that were inadequately cooked

before canning, although a number of botulism outbreaks have been traced to commercially canned foods. Once the toxin is formed, it can be destroyed only by boiling for fifteen to twenty minutes, not a common practice with canned foods. Certain fish and shellfish may also contain toxins—for example, ciguatoxin or scombroid poison—produced by bacteria or algae that the fish feed on or that grow on them, thereby poisoning the flesh for human consumption.[3]

Food may also be contaminated by the actions of food handlers, either if they themselves are infected or if they transfer pathogens from one food to another. For example, a salad might be contaminated with *Salmonella* if the raw vegetables are chopped on a cutting board that had previously been used to cut up uncooked chicken. A number of other bacterial or viral infections tend to be transferred by infected food handlers to raw or cooked foods, such as salads, hot dogs, and delicatessen takeout items. The famous case of Typhoid Mary, described in Chapter 9, illustrates how an infected food handler can spread pathogenic bacteria even when she herself has no symptoms. Hepatitis A virus is also frequently transmitted by food handlers who are careless about hygiene. The disease is most contagious ten to fourteen days before the onset of symptoms.

Government Action to Prevent Foodborne Disease

A variety of federal, state, and local agencies are responsible for protecting the safety of the food supply. Because of patchwork legislation, division of responsibility, and lack of coordination, there are major inconsistencies among different types of food in the way food safety is regulated. Increasingly, it has become clear that the system depends too heavily on detecting and correcting problems after they occur rather than preventing them. There have been a number of attempts to introduce more science-based preventive measures and increase coordination among the agencies responsible for food safety, including several bills before Congress in 2009.[11] Pending passage of legislation, however, as nutritionist Marion Nestle states in her book, *Safe Food: Bacteria, Biotechnology, and Bioterrorism*, "Today, an inventory of federal food safety activities reveals a system breathtaking in its irrationality."[12(p.55)]

The FDA and the Department of Agriculture (USDA) share the primary responsibility for ensuring that foods are safe, wholesome, and properly labeled. The laws governing the actions of the two agencies are highly inconsistent. The USDA is responsible for the safety of meat and poultry, including prepared products that contain more than 2 percent of cooked meat or poultry, as well as for processed eggs. The law requires inspection of all meat- and poultry-processing plants daily and that an inspector must be on site whenever a slaughtering plant is in operation. The plants that the USDA inspects account for about 20 percent of federally regulated foods and 27 percent of foodborne illness outbreaks. Its budget for food safety in 2009 was $972 million.[11,12]

The FDA is responsible for all other foods, including seafood and produce, which amount to about 80 percent of federally regulated foods, accounting for 67 percent of reported foodborne illness outbreaks. After increases in appropriations in 2008 and 2009, its annual budget for food safety had grown to $649 million, still far less than USDA's. Because of budgetary constraints, the FDA can inspect food processing facilities under its jurisdiction only once every ten years, on average. This leads to the paradox that a plant making frozen cheese pizza may be inspected (by the FDA) only once every ten years, while a plant making frozen pepperoni pizza will be inspected (by the USDA) almost every day. While an increasing number of outbreaks have been caused by leafy greens, the FDA does not inspect farms unless there is an outbreak. Moreover, the FDA's authority is limited: it is not mandated to review new foods before they go on the market, and it cannot order recalls of questionable products.[11] It can only request the offending company to issue a voluntary recall.

An increasing proportion of Americans' food is imported from other countries, especially developing countries, which is a challenge to the food safety system. Sixty percent of fresh fruits and vegetables and 80 percent of seafood sold in the United States are imported.[13,14] Although the USDA has the power to bar importing of meat and poultry from countries with inferior food safety systems, the FDA does not have that power for fruits, vegetables, grains, or fish. It must rely on port-of-entry inspections, an expensive and ineffective approach. The FDA inspects less than 1 percent of the imported food under its jurisdiction. Moreover, because the FDA has no authority to detain imports while testing, even if it does identify that a food is adulterated or contaminated, the food might already have been released into the U.S. food supply.[11]

President Clinton requested that Congress tighten import controls on food, but Congress failed to act.[12] Because they are eaten raw, fruits and vegetables imported from countries with inadequate safety systems are especially risky, causing, for example, the hepatitis A outbreak from Mexican green onions, the *Salmonella* outbreak from Mexican peppers, and an outbreak caused by the parasite *Cyclospora* on Guatamalan raspberries in the 1990s. As one CDC official is quoted as saying, "We used to believe you had to travel overseas to get travelers' diarrhea. It's a classic example of emerging infections common in Latin America becoming a problem here."[15]

Fish and shellfish cause more outbreaks than any other food category.[16] Regulation of the fish industry, which falls mainly under jurisdiction of the FDA, is especially difficult because most fish are caught in the wild by independent fishermen in relatively small boats. Fish may have been exposed to viruses or bacterial toxins in polluted waters, or they may have been contaminated with scombroid toxin due to inadequate cooling on the boat. Currently no

techniques are available that would allow inspectors on the docks to test for these problems. Shellfish should, in theory, be easier to regulate because their source can be determined. However, much of the enforcement is left to the states, and some of them are lax about enforcing standards.

Fish also have the potential to be contaminated with nonmicrobial toxins. Research published in 2004 revealed that farmed salmon contained potentially dangerous levels of PCBs, as well as dioxin and several organochlorine pesticides. It turned out that farmed fish were fed a concentrated feed that was tainted with the chemicals. Since the news broke, fish farmers are experimenting with new feeds that will eliminate the PCB problem.[3] Another hazard from fish was revealed in 2008, when *The New York Times* published a report that it had found high levels of mercury in sushi made from tuna in twenty Manhattan stores and restaurants.[17] It has long been known that pregnant women and children should limit their consumption of some varieties of canned tuna because they contain mercury, but the levels found in the sushi were significantly higher. Mercury gets into the ocean from industrial sources, especially coal-burning power plants, is absorbed by bacteria and makes its way up the food chain to larger fish such as tuna, as described in Chapter 19. There is controversy about the extent of the risk from farmed salmon or tuna, because the risks must be balanced against the many health benefits of eating fish. A review of the evidence published in 2006 concluded that the cardiovascular benefits of modest fish consumption—one or two servings per week—far outweigh the possible increased cancer risk for adults. The authors recommended that pregnant women, women of childbearing age, and young children should avoid swordfish, shark, golden bass, and king mackerel and should eat no more than six ounces per week of albacore tuna.[18]

Because of concerns about seafood, as well as repeated outbreaks caused by meat, including the *E. coli* outbreak from Jack-in-the-Box hamburgers in 1993, the Clinton administration implemented a new preventive approach to meat and seafood safety; which took effect in December 1997.[12] Called HACCP ("hassip"), the new system was developed in the 1960s by food processors in cooperation with the National Aeronautics and Space Administration (NASA), to ensure that foods prepared for the astronauts were safe. Rather than relying on inspections, which can never be done frequently or thoroughly enough to ensure complete safety, the HACCP system focuses on procedures, putting the responsibility on food businesses to analyze their procedures and requiring government inspectors to verify compliance. The system involves identifying potential sources of contamination and devising ways to avoid them. HACCP—which stands for "Hazard Analysis Critical Control Point"—requires an analysis of every step in the process of food production, processing, and preparation, as seen in **Box 23-1**. The purpose is to identify each possible hazard and, for each, one or more "control points," which are practices and procedures that will eliminate, prevent, or minimize the hazard.[12,14]

Box 23-1

HACCP Procedures

1. Conduct a hazard analysis
2. Determine the critical control points
3. Establish critical limits
4. Establish monitoring procedures
5. Establish corrective actions
6. Establish verification procedures
7. Establish record-keeping and documentation procedures

Source: U.S. Food and Drug Administration, "Food: Hazard Analysis & Critical Control Points (HACCP)" www.fda.gov/Food/FoodSafety/HazardAnalysisCriticalControlPointsHACCP/default.htm (Accessed November 10, 2009).

Many companies were already using HACCP, and the FDA and USDA in the late 1990s moved to encourage more reliance on the system. When fully implemented, HACCP is intended to reduce the need for inspections, relying instead on frequent reviews of procedures to make sure the system is being carried out. Although the meat and poultry industries resisted at first, the USDA reported that by 1999, 96 percent of federally regulated plants were using HACCP, including a requirement that the foods be tested for common pathogens. The FDA implemented HACCP for seafood and then added raw sprouts, eggs, and fresh juice. However, under the FDA, use of the system is voluntary, and in 1999 less than half of federally regulated seafood firms were in compliance.[19] By 2004, a review by the General Accounting Office (GAO), the investigative arm of Congress (whose name was changed later in 2004 to the Government Accountability Office), reviewed the FDA's program for the safety of imported seafood, which accounts for 80 percent of the seafood Americans consumed. The review found that the FDA's procedures were still significantly deficient. The GAO made a number of recommendations for improvement, including developing agreements with trading partners that they maintain comparable food safety systems, requiring importers to ensure that foreign firms comply with HACCP regulations, and giving enforcement priority to violations posing the most serious risks.[14]

The FDA, in addition to its oversight of food production on a national scale, issues recommendations that state and local governments can use to regulate establishments that deal with food, including retail stores, restaurants, and institutions such as schools and nursing homes. These rules emphasize the importance of hand washing by food service workers and restricting sick workers from direct contact with food. They also include strict guidelines concerning the temperatures at which food may be stored, cooked, and kept in heating trays. To prevent bacterial growth, foods should be refrigerated at 40 degrees Fahrenheit or below, or heated thoroughly so that internal temperatures are above 140 degrees. Special rules apply to large pieces such as roast meats and stuffed poultry because their internal temperatures may lag behind the external changes in temperature, allowing pathogens to grow during roasting or after refrigeration.[3] Local health departments usually enforce these rules by conducting periodic inspections of stores, restaurants, and institutions, and they are usually authorized by local and state laws to close facilities that are significantly in violation.

One potential solution to the problem of foodborne disease is the use of radiation to kill microbial contaminants in food. The idea of irradiating food frightens many people, and the proposal has aroused great opposition among some consumer groups; yet it leaves no radioactive residue, and more than forty years of research have shown it to be safe. It is already used for some foods in the United States and is widely used in some other countries. Radiation treatment kills pests in dried herbs, spices, and tea, controls insects in wheat and flour, and kills the parasites that cause trichinosis when undercooked pork is eaten. It has been shown to greatly reduce the contamination of chicken breasts with *Salmonella*, ground beef with *E. coli* 0157:H7, and shrimp with cholera bacteria. Because microbial contamination of food is such a common hazard, with potentially deadly consequences, many experts believe that widespread use of irradiation could greatly increase the safety of the food supply. The FDA has approved irradiation of red meat, poultry, pork, fruits and vegetables, seeds, herbs and spices, eggs, and wheat. In 2004, the USDA began to offer irradiated ground beef as part of the National School Lunch Program.[3,20] In 2008, the FDA approved irradiation for iceberg lettuce and fresh spinach to help protect consumers from *Salmonella* and *E. coli*.[21] All foods that have been irradiated are required to be labeled as such. Some experts believe that irradiation should be used routinely for many foods. The CDC has estimated that irradiation of high-risk foods could prevent up to a million cases of bacterial foodborne disease each year in North America.[22]

A very important component of any food safety program is epidemiologic surveillance and prompt follow-up of any foodborne outbreak to prevent further spread of disease. With a nationwide food distribution network, local public health authorities may not recognize that a number of seemingly isolated cases of an illness might be caused by contamination at a single source. The CDC has a program called PulseNet, consisting of public health laboratories in all

fifty states and Canada that can do DNA "fingerprinting" on foodborne bacteria. The network permits timely comparisons of pathogens that may cause outbreaks in various parts of the country, identifying common sources and enabling public health officials to take action to halt distribution of a contaminated food.[23]

The system worked in November 2008, when PulseNet staff noted that an unusual strain of *Salmonella* had been reported from twelve states. As CDC epidemiologists, working with state and local health departments, began to investigate the cluster of cases, more case reports flooded in. Interviews with patients suggested an association with peanut butter. After noting that several of the patients had eaten in institutional settings, including nursing homes and an elementary school, the source of the problem was identified in early January 2009 as peanut butter produced by a Georgia company, which supplied the product to institutions and to producers of other foods, including cookies, crackers, cereal, candy, ice cream, and pet treats. The company voluntarily recalled all products, leading to a cascade of recalls of peanut-butter-containing products made by other companies. As of the end of January 2009, 529 people from 43 states had been reported with laboratory-confirmed cases of the same unusual strain; 116 of them had been hospitalized and 8 had died. The outbreak was probably considerably larger than the official numbers, since only about 3 percent of *Salmonella* infections are laboratory confirmed. The Georgia plant was found to be severely deficient, with rodents, a leaky roof, demoralized workers, and previous evidence of *Salmonella* contamination that had not been addressed. The plant is now closed, and the business is under criminal investigation.[24,25]

Another program developed by the CDC is an active surveillance network, called FoodNet, designed to help public health officials better understand the epidemiology of foodborne diseases in the United States.[26] In contrast with the usual epidemiologic surveillance, called passive surveillance, in which the public health agency waits for information to be reported to it by doctors, hospitals, and laboratories, FoodNet investigators conduct active surveillance. They contact laboratories to ask about every case of diarrheal illness they conducted tests on; send surveys to physicians to determine how often and under what conditions they send stool specimens to laboratories; and even call members of the general population to ask if they have had recent diarrheal illnesses, what they think might have caused it, and whether they sought treatment. The data collected by these methods provide information on less severe foodborne illnesses that are often not reported to public health authorities and help officials at the USDA and FDA identify where their regulatory systems should be improved. The FoodNet network includes, in addition to the CDC, investigators at the USDA, the FDA, and ten state health departments. After FoodNet was implemented in 1996, the incidence of infections caused by a number of pathogens declined, but since 2004 there has been no further progress.[27]

Despite some signs of improvement, the patchwork system of federal food safety regulation remains, and there have been repeated calls to establish a single, independent agency that would administer a unified, science-based food safety system. The Institute of Medicine, the President's Council on Food Safety, and the GAO have each conducted studies on the current system and concluded that laws should be revised to give one federal official responsibility and authority to keep the nation's food supply safe. Part of the problem is resistance by the powerful food industry, which has great influence in Congress.[12] However, the need has become even more urgent since the threat of bioterrorism has become more prominent. In December 2004, when then Secretary of Health and Human Services announced his resignation, he warned of the problem. "For the life of me, I cannot understand why the terrorists have not attacked our food supply because it's so easy to do," Secretary Tommy Thompson said in his final press conference.[28]

Additives and Contaminants

Food safety standards include limits on unwanted substances that accidentally get into food—contaminants—as well as on additives, which are purposely incorporated into food to improve its taste, color, and resistance to deterioration. Contaminants that can be detected by inspection include dirt, hairs, rodent feces, and insect parts. Pesticide residues may be left on food as a result of crop spraying or when livestock eat pesticide-contaminated fodder. A pesticide law passed by Congress in 1996 requires the Environmental Protection Agency to establish tolerance levels—the maximum allowable residues—for all pesticides used on food crops. While earlier health concerns focused on cancer, the new law requires testing of pesticides for damage to the endocrine system and for effects on developing fetuses, infants, and young children. The FDA and the USDA are then required to monitor foods to ensure that pesticide residues are within the allowed tolerance levels.[29]

However, the monitoring system has been criticized because only a fraction of the food supply is tested, because tests are available for only some of the pesticides, and because when contaminants are detected, it is often too late to prevent the food from being marketed. This is especially a problem with imported foods, which may contain residues of pesticides that are banned in the United States.

Other possible contaminants include hormones and antibiotics. As discussed in Chapter 10, the use of antibiotics in livestock feed is believed to have led to increased antibiotic resistance in many bacteria. The sex hormone diethylstilbestrol, a form of estrogen, used to be fed to chickens to promote their growth. Because of concerns that hormone residues in the meat might increase human breast cancer risk, the practice was banned in 1977. In 1994, the FDA approved

the use of bovine growth hormone in dairy cows to increase their milk production. Although hormone residues are generally not found in the milk, many consumers are concerned about the safety of the practice.[3]

Many people choose foods labeled "organic," believing that these foods are safer than foods grown by common commercial methods. Until 2000, however, there was no federal standard that regulated what foods could be labeled organic. A 1990 law required the USDA to set standards, but there was so much controversy and objections from the conventional food industry that it took over a decade for the standards setting process to be completed and the standards to finally become fully effective in 2002. The standards require that organic meat, poultry, eggs, and dairy products must be grown without antibiotics or growth hormones, and organic produce must be grown without pesticides, synthetic fertilizers, or sewage sludge. Genetically engineered products and radiation are also not allowed for organic foods. Then in early 2004, the Bush administration "clarified" the standards, weakening some of the prohibitions on antibiotics and pesticides.[30,31] There was such a clamor of protest that the agriculture secretary reversed the new ruling the next day. Studies have shown that organic produce contains only one third as many pesticide residues as conventionally grown foods and that children fed organic produce and juice had only one-sixth the level of pesticide byproducts in their urine compared with those that ate conventionally farmed foods.[32,33]

Additives are put into food for a variety of reasons. One purpose is to prevent deficiency diseases that used to cause serious public health problems in the United States. For example, the addition of iodine to table salt has virtually eliminated goiter; vitamin D added to milk has done away with rickets; and niacin, a B vitamin, is added to bread to prevent pellagra. As discussed in Chapter 18, the FDA mandates that folic acid be added to flour and rice products to prevent some birth defects. Another purpose of food additives is as a preservative, to retard spoilage or prevent fats from turning rancid. Other additives are used to improve color or to enhance flavor or texture.[3]

Because of public concern about the safety of many food additives, Congress passed legislation in 1958 that required FDA approval for any proposed food additive. Additives already in use were exempted and placed on the GRAS list—"generally regarded as safe." Since then, several additives on the list have been removed because they turned out not to be safe, among them several food colors that were shown to be carcinogenic.

Drugs and Cosmetics

As its name makes clear, the FDA is also responsible for the safety of drugs. This responsibility includes both prescription drugs and over-the-counter drugs—those available without a prescription. Both types of drugs must be proven safe and effective before they can be approved by the FDA.

The FDA does not test drugs itself. Companies seeking to market new drugs are required by law to conduct the tests and submit the evidence to the agency. FDA staff then review the data and determine whether the evidence supports the new drugs' safety and efficacy.

There is an orderly procedure for collecting the evidence on new prescription drugs. Several stages of exchange of information between the pharmaceutical company and the FDA are required. The company files a new drug application (NDA) for an investigational new drug, providing evidence that the drug has the desired effect in animals and satisfies some basic safety criteria. If the FDA approves the NDA, the company is allowed to test the drug in humans in clinical trials. The trials go through three phases: In phase I, the new drug is given to a small number of people who are extensively tested to measure absorption, distribution, metabolism, and excretion, and to look for side effects and toxicities. Phase II tests a larger number of patients for signs that the new drug is effective. Phase III is a full-scale controlled trial, as described in Chapter 5, in which patients are assigned randomly to two groups. People in the experimental group receive the new drug. Members of the control group receive either a placebo or standard treatment.[34]

The FDA also has a system of postmarketing surveillance, in which doctors and patients can report adverse reactions to an approved drug. On occasion, evidence arises after a drug is on the market that it has risks that were not recognized in preapproval studies. The FDA has revoked its approval of a number of drugs based on such evidence. For years, the Agency's drug approval process has involved great political controversy, as described later in this chapter.

Cosmetics are more loosely regulated by the FDA. They do not need preapproval. In fact, there is no requirement for safety testing of cosmetics, but a warning label must be attached to any product that has not been tested. A number of ingredients that were used in the past have been shown to be harmful to health, and their use is prohibited by law. These include several chlorinated compounds as well as some color additives and most compounds containing mercury.

Food and Drug Labeling and Advertising

The scandals that inspired passage of the original Pure Food and Drugs Act of 1906 were cases of economic fraud as much as they were threats to public health. Expensive imports such as tea, coffee, and spices were frequently adulterated with dried leaves of native trees or ground native nuts and berries.[35] Thus, accurate labeling was one of the important provisions of the 1906 act. Labeling requirements have become increasingly elaborate over the years. Recently, as it has become clear that overall dietary behavior has far more impact on health than food contamination does (see Chapter 16), the FDA has placed more emphasis on empowering consumers to eat a healthy diet. Regulations established in 1994 require labels on prepared foods to contain information on fats, fiber, vitamins, and other nutrients, along with recommended daily intakes for these nutrients. Because the kinds of fats in the diet have an important effect on health, especially heart disease, labels are required to list the amount of artery-clogging saturated fat, the kind found in butter, whole milk, beef, and pork. Then, since January 2006, foods have been required to add to their labels the amount of trans fats in a serving of the product. Trans fats, which have been used since the 1980s as substitutes for saturated fats in margarine, fried foods, and baked goods, have been found to be at least as harmful to arteries as saturated fats.[36]

Accurate labels on drugs are also required by the FDA. Here the emphasis is on ensuring that claims of safety and efficacy are accurate and communicate information about hazards directly to the consumer. This is especially important for over-the-counter drugs, for which the label may be the sole basis on which consumers choose to buy and consume the product. Oddly, advertising—a form of labeling—of over-the-counter drugs is regulated by the Federal Trade Commission rather than the FDA. However, the labeling of prescription drugs falls under the authority of the FDA. Prescription drugs are increasingly being advertised directly to consumers, and critics have become concerned that these ads are often misleading, overemphasizing the benefits and deemphasizing the risks. If the FDA determines that an ad is misleading, it may send a notice of violation to the drug company; however, the agency's authority is limited, and it has been criticized for not enforcing the law vigorously.[37]

Unfounded claims for health benefits from certain foods, drugs, and vitamins have had popular appeal in the United States since the nation's birth, despite governmental efforts to enforce accuracy in labeling and advertising. In the late 19th and early 20th centuries, patent medicines contained alcohol and sometimes opium, which helped patients feel better but did little to cure the underlying problems. Still today, desperate patients suffering from incurable diseases turn to quack therapies, at best just wasting their money, but in some cases turning their backs on therapies that might do some good. The FDA can act when labels on a food or drug contain false or

misleading claims; accompanying leaflets are considered labels. However, nothing can be done to suppress articles and books containing unsubstantiated health claims about foods and "nutritional supplements" if the writings cannot be classified as labels.

Among the most persistent nutritional misconceptions has been the belief that if it is "natural," it must be safe. Accordingly, Congress in 1994 succumbed to intense lobbying by the health food industry and passed the Dietary Supplement Health and Education Act, which was signed by President Clinton. The Act forbids the FDA from requiring safety testing of herbs and food supplements. Consequently, a number of products known to have quite potent physiological effects are sold freely in health food stores, although they may turn out to be harmful once they are better understood. For example melatonin, promoted as a sleep aid and treatment for jet lag, is sold as a nutritional supplement despite the fact that it is a hormone with unknown and potentially powerful effects on the brain and the reproductive and immune systems.

In 1996, people were shocked by news stories that a college student on spring break had died after taking an herbal product called "Ultimate Xphoria" (also called "Herbal Ecstacy"), which contained ephedra, a potent natural stimulant similar to amphetamines. Ephedra-containing compounds were marketed as energy boosters, aids to weight loss, as sexual stimulants, and as a way to get high.[38] Soon afterward, the CDC reported that 8 deaths and 500 adverse health affects including heart attacks, seizures, and psychoses, had occurred nationwide among people who had consumed ephedra-containing products.[39] While some state and local governments banned these products, the FDA could not stop their sale and use. Finally, after the highly publicized death in early 2003 of a 23-year-old Baltimore Orioles pitcher who used ephedra to lose weight at the beginning of spring training, the FDA banned the substance. It was the first time that the FDA had removed a dietary supplement from the market since 1994, and the action succeeded only after the agency had reviewed some 16,000 reports of adverse reactions, commissioned a study by a nonprofit research agency, and received tens of thousands of comments from the public.[40]

Ephedra is not the only natural substance that has proven to be unsafe. According to the American Association of Poison Control Centers, between the passage of the 1994 Act and 2007, poison control centers received more than 1.6 million reports of adverse reactions to vitamins, minerals, essential oils, herbs, and other supplements. In 2005 alone, there were 2001 reports of reactions to melatonin, including 535 hospitalizations and 4 deaths. A federal law passed in 2007 requires supplement manufacturers to report serious adverse effects to the FDA; whether the law will result in significant reporting remains to be seen.[41]

Politics of the FDA

The FDA regulates products amounting to over 25 percent of consumer dollars spent in the United States.[42] Not surprisingly, it has made itself unpopular with some of the industries financially impacted by its decisions. These industries can place intense political pressures on Congress and the White House to rein in the agency's actions, as illustrated by the success of the dietary supplement industry in getting itself exempted from FDA oversight.

One of the most frequent criticisms of the FDA has been that it is too slow in approving new drugs. This complaint comes from the pharmaceutical industry, which argues that companies must wait too long to recoup their investments in research and development, as well as from patients with intractable diseases, who feel they are being denied promising new treatments. AIDS activists were especially critical of the FDA's caution, arguing that they would inevitably die if the process of new drug approval was not accelerated. Citing the thalidomide disaster that was averted in the United States by a cautious FDA official (see Chapter 12) was no longer enough to deter calls for "reform." In 1992, Congress acted to speed up the approval process by requiring drug companies to pay a fee for the processing of NDAs, which allowed the agency to hire more reviewers, but this situation has given rise to other problems, as discussed below.

Consumer advocates claim that the FDA is now too ready to approve new drugs, a claim supported by the necessity in recent years to recall several drugs because of adverse effects that became evident only after they were on the market. For example, the diet drug known as "fen-phen," approved in 1996, had to be recalled a year later because it caused serious heart valve problems.[43,44] Other drugs that were withdrawn included the allergy drug Seldane in 1997 because of cardiac arrhythmias, the diabetes drug Rezulin in 2000 because of liver problems, and the cholesterol-lowering drug Baycol in 2001, because of injury to muscle tissue.

Further doubts about the drug-approval and -monitoring process surfaced in 2004 when the Merck pharmaceutical company withdrew from the market Vioxx, a pain killer that was one of the most widely advertised drugs in the world and had earned $2.5 billion for the company since it was approved by the FDA in 1999. Merck had found in a new study that people taking the drug doubled their risk of heart attacks and strokes. Questions were raised about why the FDA had not recognized the problems with Vioxx and recalled it earlier. In a hearing by the Senate Finance Committee, FDA employees disagreed with one another on whether the agency was too likely to surrender to the demands of the industry. As described in a *New York Times* news report on the hearing, "the clash was a rare public airing of tensions that have simmered in the agency for decades."[45] The conflict is clearly one that also reflects the opposing views Congress has held on the agency. After years of congressional pressure on the FDA to protect

the interests of the pharmaceutical industry, the FDA is now accused of neglecting the safety of consumers.[45] As the newly appointed commissioner and principal deputy commissioner wrote in a 2009 article, "It has been said that the FDA has just two speeds of approval—too fast and too slow."[46]

Critics complain that since the 1992 law permitting pharmaceutical companies to pay "user fees" to speed up drug approval, the agency has become too cozy with the companies. They noted that the number of recalls of new drugs had increased dramatically, amounting to over 5 percent in the period 1997 to 2001, implying that the drugs were being approved too easily.[47] Moreover, the law has forced the FDA to spend almost 80 percent of its budget, supplemented by the user fees, for drug approvals, with too little allocated for safety monitoring after the drugs have been approved. Postmarketing surveillance relies on the drug companies to report adverse effects, a system that is inadequate at best and rife with conflicts of interest on the part of the companies. In many cases, clinical trials do not include enough patients to detect rare responses that may become evident when large numbers of people take the drug after it has been approved.

Drugs sold in the United States, like food, are increasingly being manufactured in and imported from other countries, especially China and India. The FDA has a mandate to inspect producers of drugs and chemicals used to manufacture drugs for the American market, but it has been overwhelmed with the increasing number of foreign producers, estimated as between 3200 and 6800. That challenge was illustrated by the recall in 2008 of large quantities of heparin, a blood thinner commonly used to prevent clotting during surgery or other medical procedures, because of allergic reactions to an impurity introduced during manufacture at a plant in China. At least 62 people in the United States died as a result. The Chinese plant had not been inspected by the FDA.[48]

The FDA's difficulties inspired a review by the Institute of Medicine, which recommended a number of reforms.[49] The report emphasized the need for improved monitoring of the safety of drugs after they have been approved and introduced into the marketplace. It recommended more funding for that purpose and greater authority for the FDA to require companies to conduct follow-up clinical studies on newly detected adverse effects. It also proposed that newly approved drugs should carry labeling that indicates safety information is incomplete, and that direct-to-consumer advertising should be banned for the first two years after approval. Another proposal was for the mandatory registration of clinical trials, as discussed in Chapter 6.[50]

Congress passed legislation in 2007 that addressed some but not all of the criticisms. It reauthorized the use of user fees for the drug approval process, and it also significantly increased funding for postmarketing studies of drugs already on the market. It granted the agency authority to require companies to do studies on approved drugs for adverse side effects. The law re-

quires registration of all clinical trials and public posting of their results. It includes incentives for testing drugs in children, as well as provisions designed to limit conflicts of interest of advisors. However, it did very little to address concerns about the safety of imported foods.[51]

Conclusion

Confidence in the safety of the U.S. food supply has been shaken in recent years by widely publicized outbreaks of illnesses caused by foods, ranging from bagged spinach to peanut butter. Common sources of illness include *Salmonella* bacteria in poultry, meat, and eggs, as well as a variety of viruses and parasites in fish and shellfish. Over the past two decades, *E. coli* 0157:H7 has emerged as a serious threat in ground beef and other foods as well as in unpasteurized fruit juice.

Governmental responsibility for food safety is distributed among a variety of federal, state, and local agencies. The laws are inconsistent and, in many cases, paradoxical. The USDA has significant authority over meat and poultry safety. The FDA is responsible for most other foods, including fish and seafood, but its financial resources for inspection and monitoring are limited, and it has little power to act. The increasing proportion of imported foods in the American market has posed serious challenges to food safety regulation.

As the problem of food contamination became more apparent in the 1990s, the focus of the FDA and the USDA has fallen on a system for preventing problems before they occur rather than depending on inspections to detect food that is already contaminated. The system, called HACCP, analyzes every step in the process of food production, processing, and preparation, with the objective of identifying possible hazards and instituting practices that will eliminate or minimize them. The FDA has approved irradiation of many foods to kill microbial contaminants. Although many consumers are distrustful of irradiated food, the practice has been shown to be safe, and many experts believe routine irradiation would greatly improve the safety of our food supply. Strengthened surveillance for rapid detection of foodborne disease outbreaks is another feature of the food safety system; in the event of an outbreak, surveillance allows sources to be identified so that they can be halted rapidly.

In addition to its role in the prevention of microbial contamination of food, the FDA regulates food additives and chemical contaminants, as well as food labeling and advertising. It sets standards for foods to be labeled "organic."

The FDA also has oversight of the safety of drugs and medical devices. This responsibility has led to considerable controversy as the pharmaceutical industry and patient groups complain about the slow pace of new drug approval. Conservatives in Congress have made repeated efforts to weaken the agency's authority and to force it to act more quickly on drug approvals. One result was legislation passed in 1992 that allowed the FDA to assess fees on the pharma-

ceutical industry to be used for processing new drug approvals. Critics believe that this practice has led to too cozy a relationship between the agency and the drug companies. Another law that has been controversial is the Dietary Supplement Health and Education Act of 1994, which prohibits the FDA from regulating herbs and food supplements. Consumer groups are concerned that these laws, together with the climate of pressure to speed up drug approvals, endanger public health by allowing unsafe products on the market.

Several scandals occurred in the late 1990s and the 2000s that confirmed fears that drugs are approved too easily and that the system for detecting safety problems after approval is inadequate. Increasing importation of drugs from foreign countries has made regulation more difficult. Evidence that pharmaceutical companies selectively publicize clinical trials that show benefits of their drugs while suppressing negative results led to mandatory registration of clinical trials at the outset, so that all the evidence will be available publicly. This requirement was part of legislation passed in 2007 that also included a number of other measures designed to increase the FDA's funding and authority. Whether these measures will be effective in improving the safety of pharmaceuticals remains to be seen.

References

1. P. S. Mead et al., "Food-Related Illness and Death in the United States," *Emerging Infectious Diseases Journal* 5 (1999): 607–625.
2. W. M. Laydon, "Food Safety: A Patchwork System," *GAO Journal* (Spring–Summer 1992): 48–59.
3. A. Nadakavukaren, *Our Global Environment: A Health Perspective*, 6th ed. (Prospect Heights, IL: Waveland Press, 2005).
4. C. Drew and P. Belluck, "Deadly Bacteria—a New Threat to Fruit and Produce in U.S.," *The New York Times*, January 4, 1998.
5. P. Belluck and C. Drew, "Tracing Bout of Illness to Small Lettuce Farm," *The New York Times*, January 5, 1998.
6. T. Breuer et al., "A Multistate Outbreak of *Escherichia coli* 0157:H7 Infections Linked to Alfalfa Sprouts Grown from Contaminated Seeds," *Emerging Infectious Diseases Journal* 7 (2001): 977–982.
7. Center for Science in the Public Interest, "CSPI Outbreak Alert Data: Info on Produce Outbreaks," www.cspinet.org/new/pdf/cspi_outbreak_alert.pdf, 2006, accessed August 22, 2009.
8. L. Polgreen, "Hepatitis Inquiry Moves Deliberately from Farm to Plate," *The New York Times*, November 18, 2003.
9. D. W. K. Acheson and A. E. Fiore, "Preventing Foodborne Disease—What Clinicians Can Do," *New England Journal of Medicine* 350 (2004): 437–440.
10. U.S. Centers for Disease Control and Prevention, "Outbreak of *Salmonella* Serotype Saintpaul Infections Associated with Multiple Raw Produce Items—United States, 2008," *Morbidity and Mortality Weekly Report* 57 (2008): 929–934.

11. C. S. DeWaal and D. W. Plunkett, Center for Science in the Public Interest, "Building a Modern Food Safety System for FDA Regulated Foods," www.cspinet.org/new/pdf/fswhitepaper.pdf, May 2009, accessed August 23, 2009.
12. M. Nestle, *Safe Food: Bacteria, Biotechnology, and Bioterrorism* (Berkeley, CA: University of California Press, 2003).
13. U.S. Government Accountability Office, "Revamping Oversight of Food Safety." www.gao.gov/transition_2009/urgent/food-safety.php, June 10, 2008, accessed August 23, 2009.
14. U.S. General Accounting Office, "FDA's Imported Seafood Safety Program Shows Some Progress, but Further Improvements Are Needed," www.gao.gov/new.items/d04246.pdf, January 2004, accessed August 24, 2009.
15. M. Burros, "President to Push for Food Safety," *The New York Times*, July 4, 1998.
16. Center for Science in the Public Interest, "Fish and Shellfish top CSPI Outbreak List," www.cspinet.org/new/200811251.html, November 25, 2008, accessed August 23, 2009.
17. M. Burros, "High Mercury Levels Are Found in Tuna Sushi Sold in Manhattan," *The New York Times*, January 23, 2008.
18. D. Mozaffarian et al., "Fish Intake, Contaminants, and Human Health: Evaluation the Risks and the Benefits," *Journal of the American Medical Association* 296 (2006): 1885–1899.
19. R. A. Robinson, "Food Safety and Security: Fundamental Changes Needed to Ensure Safe Food," General Accounting Office, Testimony Before the Subcommittee on Oversight of Government Management, Restructuring and the District of Columbia, Committee on Governmental Affairs, U.S. Senate. October 10, 2001, www.gao.gov/new.items/d0247t.pdf, accessed August 23, 2009.
20. M. T. Osterholm and A. P. Norgan, "Role of Irradiation in Food Safety," *New England Journal of Medicine* 350 (2004): 1898–1901.
21. U.S. Food and Drug Administration, "Irradiation: A Safe Measure for Safer Iceberg Lettuce and Spinach," www.fda.gov/ForConsumers/ConsumerUpdates/ucm093651.htm, August 22, 2008, accessed August 25, 2009.
22. D. G. Maki, "Coming to Grips with Foodborne Infection—Peanut Butter, Peppers, and Nationwide Salmonella Outbreaks," *New England Journal of Medicine* 360 (2009): 949–953.
23. U.S. Centers for Disease Control and Prevention, "What Is PulseNet?" www.cdc.gov/PULSENET, April 28, 2009, accessed August 25, 2009.
24. U.S. Centers for Disease Control and Prevention, "Multistate Outbreak of *Salmonella* Infections Associated with Peanut Butter and Peanut Butter-Containing Products—United States, 2008–2009," *Morbidity and Mortality Weekly Report* 58 (2009): 85–90.
25. M. Moss, "Peanut Case Shows Holes in Food Safety Net," *The New York Times*, February 9, 2009.
26. U.S. Centers for Disease Control and Prevention, "FoodNet—Foodborne Diseases Active Surveillance Network," www.cdc.gov/foodnet/, August 13, 2009, accessed August 25, 2009.
27. U.S. Centers for Disease Control and Prevention, "Preliminary FoodNet Data on the Incidence of Infection with Pathogens Transmitted Commonly Through Food—10 States, 2008," *Morbidity and Mortality Weekly Report* 58 (2009): 333–337.

28. R. Pear, "Departing Health Secretary Warns of Flu Risk and Attacks on Food," *The New York Times*, December 3, 2004.
29. U.S. Environmental Protection Agency, "Accomplishments under the Food Quality Protection Act (FQPA)," www.epa.gov/pesticides/regulating/laws/fqpa/fqpa_accomplishments.htm, August 3, 2006, accessed August 25, 2009.
30. M. Burros, "Last Word on Organic Standards, Again," *The New York Times*, May 26, 2004.
31. M. Burros, "Agriculture Dept. Rescinds Changes to Organic Food Standards," *The New York Times*, May 27, 2004.
32. M. Burros, "Study Finds Far Less Pesticide Residue on Organic Produce," *The New York Times*, May 8, 2002.
33. C. K. Yoon, "Exposure to Pesticides is Lowered When Young Children Go Organic," *The New York Times*, March 25, 2003.
34. U.S. Food and Drug Administration, "The FDA's Drug Review Process: Ensuring Drugs Are Safe and Effective," www.fda.gov/Drugs/ResourcesForYou/Consumers/ucm143534.htm, July 10, 2009, accessed August 27, 2009.
35. R. M. Deutsch, *The New Nuts Among the Berries: How Nutritional Nonsense Captured America* (Palo Alto, CA: Bull Publishing, 1977).
36. U.S. Food and Drug Administration, "Talking About Trans Fat: What You Need to Know," www.fda.gov/Food/ResourcesForYou/Consumers/ucm079609.htm, May 2006, accessed August 25, 2009.
37. S. M. Wolfe, "Direct-to-Consumer Advertising—Education or Emotion Promotion?" *New England Journal of Medicine* 346 (2002): 524–526.
38. M. Burros and S. Jay, "Concern Grows Over Herb That Promises a Legal High," *The New York Times*, April 10, 1996.
39. U.S. Centers for Disease Control and Prevention, "Adverse Events Associated with Ephedrine-Containing Products—Texas, December 1993–September 1995," *Morbidity and Mortality Weekly Report* 45 (1996): 689–692.
40. S. G. Stolberg, "U.S. To Prohibit Supplement Tied to Health Risks," *The New York Times*, December 31, 2003.
41. D. Hurley, "Diet Supplements and Safety: Some Disquieting Data," *The New York Times*, January 16, 2007.
42. A. J. J. Wood, "Playing 'Kick the FDA'—Risk-free to Players but Hazardous to Public Health," *New England Journal of Medicine* 358 (2008): 1774–1775.
43. J. Couzin, "Gaps in the Safety Net," *Science* 307 (2005): 196–198.
44. W. A. Ray and C. M. Stein, "Reform of Drug Regulation—Beyond an Independent Drug-Safety Board," *New England Journal of Medicine* 354 (2008): 194–201.
45. G. Harris, "FDA Failing in Drug Safety, Official Asserts," *The New York Times*, November 19, 2004.
46. M. A. Hamburg and J. M. Sharfstein, "The FDA as a Public Health Agency," *New England Journal of Medicine* 360 (2009): 2492–2495.
47. P. B. Fontanarosa, D. Rennie, and C. D. DeAngelis, "Postmarketing Surveillance—Lack of Vigilance, Lack of Trust," *Journal of the Medical Association of America* 292 (2004): 2647–2650.

48. S. O. Schweitzer, "Trying Times at the FDA—The Challenge of Ensuring the Safety of Imported Pharmaceuticals," *New England Journal of Medicine* 358 (2008): 1773–1777.
49. Institute of Medicine, *The Future of Drug Safety: Preserving and Protecting the Health of the Public* (Washington, DC: National Academies Press, 2006).
50. G. D. Curfman, S. Morrissey, and J. M. Drazen, "Blueprint for a Stronger Food and Drug Administration," *New England Journal of Medicine* 355 (2006): 1821.
51. G. Harris, "House Passes Bill Giving More Power to the FDA," *The New York Times*, September 20, 2007.