SOCIAL ISSUES IN AMERICA
AN ENCYCLOPEDIA

VOLUME THREE

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FOOD AND DRUG SAFETY

Mad cow disease, the dangers of genetically modified foods, and deadly viruses such as SARS have captured newspaper headlines in recent years. While such stories represent legitimate threats to public health, the problems of unsafe foods and drugs are perhaps less sensational but more widespread. The Centers for Disease Control (CDC) estimate that there were roughly 76 million cases of foodborne illness annually in the United States in the early 2000s. Most are mild, but an estimated 325,000 persons are hospitalized and 5,000 die each year from these illnesses.

The situation is even worse in the developing world, where the incidence of infection is much higher and the consequences more dire. The World Health Organization (WHO) estimates that 20 million persons die each year from contaminated food and water, 2 million of whom are children under the age of 5. Food safety is not a negligible concern even in the developed world, but it is a serious matter among poorer nations.

Pharmaceutical drugs present their own set of dangers. Highly processed or artificially created, most modern drugs do not contain the bacteria, viruses, or parasites that are the main causes of foodborne disease. The dangers of drugs come, instead, from their side effects, that is, the harms they inflict as they fight an illness or treat its symptoms. Nearly all drugs inflict some form of harm, which is why they should be used with care. Even in the intensive testing environment of the United States, the Office of Drug Safety received reports of 370,000 adverse reactions to prescribed drugs in the year 2003; they classified 213,000 as serious. The office does not estimate the number of unreported adverse reactions, but it is safe to assume it runs into the millions.

CLASSIFICATION OF UNSAFE FOOD AND DRUGS

The dangers from food fall into three main categories. Foreign substances in foods can harm the human body. These substances can be chemical (pesticides, lead, arsenic) or organic (bacteria, viruses, parasites). Botulism, cholera, and giardiasis are diseases caused by microorganisms. These foreign substances may cause immediate sickness or death, as botulism does, or they may impair health over longer periods, as the buildup of lead in the body does.

A second category of danger involves the quantities or proportions of food eaten. Malnutrition from inadequate intake weakens the body’s immune system and contributes to many illnesses. If the proportions of essential nutrients consumed are unbalanced, the person may have nutritional deficiency diseases such as beriberi, scurvy, and pellagra. Eating too much or improper types of food contributes to obesity, diabetes, and perhaps many forms of cancer.

The third category of danger involves food allergies. Foods that are beneficial to most people are poisonous to some; severe allergic reactions to peanuts, milk, wheat, corn, and other everyday foods are not rare.

Drugs, or medicines, have risks similar to those found in foods. Sometimes, albeit rarely, drugs may contain impurities that harm health. In 1982, Tylenol laced with arsenic killed seven persons in the Chicago area, an apparent act of product tampering. In 1988, a batch of tryptophan, an amino acid sold over the counter as a dietary supplement in the United States, contained a genetically engineered bacterium that killed 37 persons and permanently disabled 1,500 others. Another drug-related danger comes from contaminated needles used to inject illegal drugs; heroin users are at risk of contracting autoimmune deficiency syndrome (AIDS) and hepatitis this way. Even drugs that are pure and administered properly sometimes have severe adverse effects; thalidomide, for example, a drug prescribed as a tranquilizer in the 1950s and 1960s, causes birth defects in pregnant women. The proper dosage of
<table>
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<tr>
<th>Year</th>
<th>Event</th>
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<tr>
<td>2800 B.C.E.</td>
<td>First extant written record of drug prescription is created in China.</td>
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<td>ca. 500-400 B.C.E.</td>
<td>Ancient Greek physician Hippocrates establishes first rational, as opposed to mystical, approach to medicine.</td>
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<td>ca. 50-70 C.E.</td>
<td>Greek physician Dioscorides publishes <em>De Materia Medica</em>, five volumes prescribing drugs for various ailments; it is the first compilation of drug descriptions in the Western world.</td>
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<td>1618</td>
<td>The Royal College of Physicians in London publishes the first pharmacopoeia in the English language.</td>
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<td>1674</td>
<td>Dutch biologist Antoni van Leeuwenhoek invents the microscope and becomes the first to see bacteria.</td>
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<td>1796</td>
<td>English scientist Edward Jenner succeeds in developing the first safe smallpox vaccine.</td>
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<td>1810</td>
<td>Canning process for preserving food is invented by French scientist Nicolas Appert.</td>
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<td>1860</td>
<td>Britain passes first national law prohibiting adulteration of food.</td>
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<td>1862</td>
<td>The Bureau of Chemistry, predecessor of the Food and Drug Administration, is founded within the Department of Agriculture.</td>
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<td>1864</td>
<td>French microbiologist Louis Pasteur invents process of using heat to kill bacteria in food (pasteurization).</td>
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<tr>
<td>1870-1914</td>
<td>National and international food processing firms emerge in the United States and Europe. Widespread milk pasteurization begins in the United States.</td>
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<td>1905</td>
<td>Drinking water is first chlorinated in Britain.</td>
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<td>1906</td>
<td>Congress passes the Meat Inspection Act and Pure Food and Drugs Act to ensure the safety of the country’s food and drug supplies.</td>
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<td>1927</td>
<td>The Bureau of Chemistry is divided into two branches, the Bureau of Chemistry and Soils and the Food, Drug, and Insecticide Administration; the latter shortens its name to the Food and Drug Administration (FDA) in 1930.</td>
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<td>1935</td>
<td>Protonsil, the first antibiotic, is discovered to fight staphylococcal infections.</td>
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<td>1938</td>
<td>Congress passes the Food, Drug, and Cosmetic Act; among its provisions are requirements that drug companies provide scientific proof of the safety of new drugs; it also extends FDA control over cosmetics and therapeutic devices.</td>
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<td>1944</td>
<td>Penicillin is first used to treat battlefield injuries.</td>
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<td>1954</td>
<td>First widespread distribution of polio vaccines to American children occurs.</td>
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<td>1958</td>
<td>Congress passes the Food Additives Amendment, requiring manufacturers to prove the safety of food additives; the so-called Delaney proviso of the law prohibits the approval of any food additive shown to cause cancer in animals or humans.</td>
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<td>1962</td>
<td>The sleeping pill thalidomide is shown to cause major birth defects in Western Europe, and the FDA keeps the drug out of the United States.</td>
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<td>1970</td>
<td>The Environmental Protection Agency (EPA) is established and takes over regulation of pesticides from the FDA.</td>
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<td>1982</td>
<td>Tylenol laced with cyanide at Chicago-area supermarkets kills seven, resulting in stricter packaging rules and practices for food and over-the-counter drug products.</td>
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<td>1994</td>
<td>Approximately 225,000 ice cream eaters are poisoned by <em>Salmonella enteritis</em> in the worst food poisoning case in American history. The first genetically modified food product, the Flavr Savr tomato, is made available to U.S. consumers.</td>
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<tr>
<td>1995</td>
<td>World Trade Organization establishes international sanitary regulations for food and drugs.</td>
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| 2003 | The European Union passes the strictest rules on genetically modified food in the world.
Agriculture ensured a more predictable and greater supply of food, leading to gains in human population, laying the foundation of modern human civilization. The advent of agriculture—that is, the raising of crops and breeding of livestock—began about 12000 B.C.E., laying the foundation of modern human civilization. Agriculture ensured a more predictable and greater supply of food, leading to gains in human population. But agriculture was not without its drawbacks, including declines in the quality of food and human health. For example, while meats contain all of the amino acids essential to human health, grains such as rice, wheat, and corn, do not. Moreover, repeated use of the same soil can deplete healthful minerals and vitamins in food. Both of these influences likely led to increases in diseases caused by deficiencies of essential nutrients. Also, agriculture-based societies brought human populations into more concentrated settlements around water supplies, resulting in closer contact with each other and with domesticated animals. These changes led to increasing transmission of illnesses and a decline in the average level of health. Anthropologists attribute widespread anemia in Europe, Asia, and America, even among people with adequate amounts of iron in their diet, to chronic bacterial and parasitic infection.

Use of drugs may go back as far as that of food, though no fossil record has yet been uncovered. In any event, poppy seeds, from which opium is derived, were found in a grave in Granada dating from 3000 B.C.E. Egyptian records from 1500 B.C.E. prescribe drugs for various ailments; the known use of drugs in China dates from about 1100 B.C.E. (although some attribute a book on drug prescriptions to Shen Nung, the Red Emperor, in 2800 B.C.E.) and in India from about 600 B.C.E. The conquering Spanish destroyed records of the native populations in the Americas, so little is known about their early drug use; quinine and nicotine, however, were brought to Europe from the New World after Columbus’s voyages. In the first century C.E., Dioscorides, a physician from Anatolia (now part of Turkey), published a five-volume work prescribing medicines for various ailments. The prescriptions are so inaccurate by modern standards that it is impossible to weigh the early benefits and harms from their use. Some drugs no doubt helped the afflicted; antibacterial molds and copper preparations, for example, probably helped fight wound infections.

The Reformation brought the spirit of science to food and drugs in Europe. The use of his remarkable microscopes enabled Antoni van Leeuwenhoek (1632-1723) to identify bacteria for the first time. Over the next two and a half centuries, scientists proved that microbes were the causal agents in many diseases as well as food spoilage, and they developed remedies. The effort involved brilliant discoveries from across Europe—Lazzaro Spallanzani (1729-1799) from Italy, Edward Jenner (1749-1823) from England, Louis Pasteur (1822-1895) from France, and Robert Koch (1843-1910) from Germany are among the best known, but many others also contributed. The principle of “spontaneous generation” was the focus of much debate during this period. Prior to the nineteenth century, most educated persons believed microbial pathogens came to life spontaneously in plants and animals. Microbiologists were eventually able to establish, through a series of ingenious experiments, that pathogens had to be transmitted from one organism to another. This insight was crucial for the control of foodborne diseases, indicating that quarantining contaminated organisms could prevent pathogens from affecting other organisms.

In 1618, the Royal College of Physicians in Britain issued a pharmacopoeia, a list of medicinal drugs and their chemical compositions, with instructions for testing purity and strength. The practice spread to the rest of Europe and to America. During the eighteenth and nineteenth centuries, new drugs were identified and known ones isolated. Joseph Priestly discovered nitrous oxide in 1772, although it was not used as an anesthetic until later. In 1785, digitalis was discovered as a treatment for dropsy, a swelling of the limbs. Opium was isolated from poppy seeds in 1806, quinine from cinchona in 1818, and salicylic acid (similar to aspirin) from willow bark in 1838.

Drugs that killed pain and prevented infection were crucial to the development of surgery. Nitrous oxide was first used in surgery in 1842 by a Georgia doctor named Crawford Long. Ether was used in Boston for dental surgery in 1846, and cocaine was used as a topical anesthetic for eye surgery in 1848. Oliver Wendell Holmes coined the term “anesthesia” to describe the effects of these new drugs. In 1853, British physician John Snow used chloroform to assist
Queen Victoria in childbirth, popularizing its use when the Queen sang its praises. In 1857, Joseph Lister identified bacteria as the cause of gangrene, a common consequence of surgery, and successfully used carbolic acid as an antiseptic in 1867.

Despite their benefits, drugs posed dangers. Patients often died from too much mercury, which was widely used to treat syphilis in the seventeenth century. Chloroform is toxic to the liver; opium is addictive in most people, even if used for only a few weeks. Arsenic compounds, though known to be poisonous, were commonly used to treat malaria because they were cheaper than quinine. The identification of pharmacological properties of drugs greatly improved medicinal treatments, but doctors and scientists were not able to eliminate their harmful effects, nor have the advances of modern science.

Diseases caused by a deficiency of nutrients were identified in the early eighteenth century. In 1747, when James Lind, a British naval surgeon, demonstrated through clinical trials that a deficiency of citrus fruit caused scurvy, the British admiralty (after a lag of 50 years) prescribed a regimen of lime juice for its sailors (known as "Limeys"). Cures for beriberi (caused by thiamin deficiency), pellagra (lack of niacin), anemia (lack of iron), osteoporosis (lack of calcium), and other deficiency diseases were discovered during the nineteenth and twentieth centuries.

Government regulation of foods and drugs may have been practiced in preliterate societies, but contemporary knowledge is limited to written records—such as kosher laws in the Hebrew Bible and the legal codes of Babylon that regulated the planting, growing, and harvesting of grain. Historically, however, most government regulation of food and drugs has been concerned with fraud—such as cheating on quantity or weight, substituting cheap for expensive ingredients, and making unjustified claims—although some laws, such as the mixing of fresh and spoiled butter, or the sale of unwholesome wine, were concerned with safety. In 1345, the mayor of London required parts of the Thames from which drinking water was drawn to be free of dung or other filth.

The first national food law was passed in Britain in 1860, prohibiting adulteration. In 1872 the law made it a crime to mix "any injurious or poisonous ingredient" into food.

In America, Massachusetts passed a statute prohibiting the sale of unwholesome food in 1785, and over the next century and a quarter, most states enacted laws prohibiting adulteration. In 1906, Congress passed the nation's first two federal food and drug laws: the Meat Inspection Act and the Pure Food and Drugs Act. The former prohibited interstate traffic in meats that were "unsound, unhealthful, unwholesome, or otherwise unfit for human food," and provided for government inspections. The Pure Food and Drugs Act prohibited the "manufacture, sale, or transportation of adulterated or misbranded or poisonous or deleterious foods, drugs, medicines, and liquors," and likewise provided for government inspection of foods and prosecution of violators.

Neither of the measures was precipitated by an outbreak of poisoning. The Meat Inspection Act was largely a response to Upton Sinclair's novel *The Jungle*, in which he hoped to foment a socialist revolution by drawing attention to the fetid working conditions in the packinghouses. Instead, he raised concern about the safety of meat. "I aimed at the public's heart, and by accident I hit it in the stomach," he wrote. The Pure Food and Drugs Act was a response to sensational journalism and the politicking of Harvey Wiley, a government scientist who agitated against food adulteration. His campaign for safe food was politically effective, although he presented scant evidence that foods or drugs were unsafe.

By contrast, the expansion of the law in the Food, Drug, and Cosmetic Act of 1938—which, among other things, required drug manufacturers to provide scientific proof of their products' safety before putting them on the market—was precipitated by an outbreak of poisoning. In 1937, seventy-six persons died after taking sulphanilamide, a drug effective in fighting streptococcal infection. Death was caused by a manufacturer suspending the drug in ethylene glycol (antifreeze), a sweet-tasting but poisonous liquid. The deaths contributed to passage of a stronger law and more rigorous requirements for testing drugs.

Although the Pure Food and Drugs Act of 1906, the Harrison Narcotics Act of 1914, and the Food, Drug, and Cosmetic Act of 1938 established the main regulatory framework in the United States, the regulation of food and drugs has been modified and expanded over the years. The thalidomide deformities in Europe led Congress to pass the Kefauver-Harrison amendments in 1962, requiring companies to prove a drug was safe and effective before offering it to the public. In 1980, the Infant Formula Act empowered the FDA to regulate nutritional and safety standards for that product. In 1990, Congress required all packaged foods to bear a nutritional label. And the Bioterrorism Act passed in 2002 required the FDA
to inspect foods more frequently and to devise methods for the rapid detection of intentionally adulterated foods. These laws, as extended, constitute the main federal regulation of drugs in the United States.

MODERN FOOD AND DRUG INDUSTRIES

The food and drug industries in the United States today are large, complex, and dependent on international trade. In 2004, the United States traded more than $100 billion worth of agricultural goods in international markets and exported more than $21 billion in medical and pharmaceutical preparations. Both industries consist of firms that operate for profit, consumers who exercise a large degree of autonomy in purchases, and regulators that exercise local, state, national, or supranational governmental authority.

The scientists are vital to the food and drug industries and are employed by nonprofit organizations and universities, as well as firms and government agencies. All of these groups affect food and drug safety, but the primary influence is exerted by consumers. As purchasers of food and drugs, consumers want products that are safe. Of course, safety is not an absolute condition; consumers understand that there are risks, but they want those risks minimized. The demand for safe foods and drugs provides the impetus for taking precaution in the growth, processing, and distribution of these products. Consumer demand is also the rationale for regulators passing laws to govern the activities of food and drug firms, and it guides scientists’ efforts to find safe cures for diseases and improvements in food safety.

Consumers

The incentive for companies to deliver safe foods and drugs is strong because large sums of money are at stake. American consumers spent $1.1 trillion on food in 2004. They spent an additional $1.4 trillion on medical care, $250 billion on drugs. Although profits vary from year to year, in 2000 farms earned $1.2 billion, food manufacturers $27 billion, and the healthcare industry about $26 billion. In 2004, food expenditures accounted for 14 percent of all consumer expenditures in the United States, compared to 6 percent for clothes, 14 percent for housing, and 12 percent for transportation. Medical expenditures accounted for 18 percent of consumer expenditures and drugs for 3 percent. Of the 2004 expenditures for food, about $55 billion went to imported foodstuffs.

As these statistics show, the food and drug industries in the United States are enormous. Although more money is being spent on food now than in the past, that money represents a smaller portion of the family budget. In 1930, 25 percent of consumer expenditures were for food. That percentage climbed to 34 percent during the war year of 1944, then gradually declined to 25 percent by 1960, 20 percent in 1980, and 14 percent by 2000. American consumers are spending increasing amounts of their food budget outside the home. In 1929, Americans spent 16 percent of their food budget eating out; by 1950 the figure had risen to 23 percent, and by 2001 to 41 percent. These trends reflect the growing wealth of U.S. citizens, the efficiency of the nation’s prepared food industry, and the increased prevalence of the two-worker family, which leaves less time for preparing meals at home but creates more disposable income.

Opportunity trends characterize drug and medical expenditures. Americans are consuming drugs in ever-greater quantities. In 1929, drugs constituted 0.8 percent of total consumer expenditures, compared to 2.5 percent in 2001. However, the percentage has grown rapidly of late. It took more than 50 years, from 1943 to 1997, for drug expenditures to climb from 1 percent to 2 percent of consumer spending, but in only 6 years it climbed from 2 percent to 3 percent. Even so, expenditures on drugs have climbed less rapidly than medical care expenses as a whole. Expenditures on medical care represented 4 percent of total consumer spending in 1930 but 17 percent in 2003. Of the many factors involved in this increase, some of the most important are an aging population, better and more expensive medical equipment, and higher drug research costs.

Businesses

The vast amounts of foods and drugs purchased in the United States are supplied by profit-seeking enterprises. Food industry companies undertake seven primary activities from plough to plate: growing and harvesting, processing, transporting, storing, wholesaling, retailing, and preparing (restaurants) of food. Safety is important in all stages, because contamination can take place anywhere along the chain. Farmers use pesticides, some of which are harmful; soil and water can contain poisonous chemicals or biological agents; animals can carry dangerous bacteria in their digestive tracts, as well as their hair, feathers, and skin, and these bacteria can enter the edible
portions of the animal during slaughter and preparation; contaminants can enter foods while they are being transported (one of the largest outbreaks of salmonella poisoning in the United States was the result of careless transporting of ice cream); processing equipment can carry pathogens or harmful chemicals that are transferred to foods; finally, people who handle food at various stages of production as well as in the home can transmit diseases through improperly cleaned hands, hair, or clothes.

Each stage of the food industry is structured differently and thus has different associated food risks. In 2003, there were 2.127 million farms in the United States, with an average size of 441 acres. Although the trend is toward larger units (3.2 million farms had an average size of 352 acres in 1964), no small group of farmers dominates the production of wheat, corn, rice, pigs, cattle, poultry, or milk. Food is touched by many hands in the production process, leaving many opportunities for contamination. Offsetting this disadvantage is the gain that, should a batch of food contain poisonous chemicals or destructive bacteria, the number affected will not be large—a few hundred rather than a few hundred thousand.

The same is true of the trucking and restaurant businesses. Trucking and warehousing in America employed more than 2 million workers in 2004, and the wholesale trade at least another 7 million, perhaps half of whom handled food. More than 11 million workers were employed in nearly 1 million restaurants and bars, and almost half of all adults (46 percent) ate at a restaurant during the course of the average day. The opportunities for contamination are obviously large, but the chances that any particular case of contamination will affect large numbers is likely to be small.

Whereas the growth and harvesting of food products is dispersed among many firms, the manufacture of many kinds of food is not; most food manufacture is concentrated. One measure of economic concentration is the percentage of output produced by the four largest firms in an industry. The four largest U.S. firms refine 99 percent of the sugar, make 83 percent of the breakfast cereal, and process 53 percent of the butter and 32 percent of the ice cream. Animal processing is also concentrated. The four largest firms slaughter 41 percent of poultry in the United States and similar percentages of cattle and hogs. Contamination from a large manufacturing plant or slaughterhouse can affect many thousands of persons, as happened with an outbreak of salmonella poisoning in 1994. A nationally branded ice cream maker had its ingredients shipped in tanker trucks. Although the company used pasteurized ingredients, they were shipped in tanks that had previously carried unpasteurized liquid eggs. Salmonella enteritidis, a bacteria in the eggs, remained in the tanker trucks, infecting the ice cream. Despite the cleanliness of the plant itself, where no salmonella was found, contaminated ice cream was distributed nationally from a plant in Minnesota. An estimated 224,000 persons were poisoned from this source.

The danger of poisoning large numbers of customers, and the consequent decline of revenues and profitability, leads manufacturing firms to take precautions against contamination. Firms use sophisticated techniques to detect and eliminate harmful substances. Established techniques such as sampling and growing bacteria in a culture are used, but so are gene probes and other new methods designed to speed up detection. The design, use, and care of equipment, the materials and layout of the plant, the steps in processing, and the behavior of employees are subjected to close scrutiny by food companies.

Table 1. Incidence of Infections from Foodborne Pathogens, 1996–2003*

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<tbody>
<tr>
<td>Bacteria</td>
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<tr>
<td>Campylobacter (per 100,000 persons)</td>
<td>21.7</td>
<td>12.6</td>
<td>12.3</td>
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<tr>
<td>Escherichia coli (per 100,000 persons)</td>
<td>2.3</td>
<td>1.1</td>
<td>1.0</td>
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<tr>
<td>Listeria (per 1 million persons)</td>
<td>4.9</td>
<td>3.3</td>
<td>2.5</td>
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<tr>
<td>Salmonella (per 100,000 persons)</td>
<td>13.5</td>
<td>14.5</td>
<td>6.8</td>
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<tr>
<td>Shigella (per 100,000 persons)</td>
<td>7.7</td>
<td>7.3</td>
<td>N/A</td>
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<tr>
<td>Vibrio (per 1 million persons)</td>
<td>2.4</td>
<td>3.0</td>
<td>N/A</td>
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<tr>
<td>Yersinia (per 1 million persons)</td>
<td>8.9</td>
<td>4.0</td>
<td>N/A</td>
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<tr>
<td>Parasites</td>
<td></td>
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<tr>
<td>Cryptosporidium (per 1 million persons)</td>
<td>26.8</td>
<td>10.9</td>
<td>N/A</td>
<td></td>
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<tr>
<td>Cyclospora (per 1 million persons)</td>
<td>1.6</td>
<td>0.3</td>
<td>N/A</td>
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* Based on Centers for Disease Control’s Foodborne Diseases Active Surveillance Network for nine states: California, Colorado, Connecticut, Georgia, Maryland, Minnesota, New York, Oregon, and Tennessee.

These practices and improvements are often undertaken by firms that want to win customers and earn profits.

In addition to local building codes, health regulations, and national rules and inspections, a large community of private biologists, chemists, and engineers pay close attention to safety quite apart from regulators. Equipment is made from materials, such as stainless steel, that are easy to clean and disinfect. Gauges are mounted so that bacteria and viruses cannot collect in dead spaces. Even details like rubber O-rings are carefully specified, because moisture can collect and bacteria can grow around the edges. Buildings are constructed to discourage bird nesting; outside lights are placed away from the buildings because they attract insects; humidity is kept low to prevent molds; floors are kept dry; and administrative offices are separated from processing areas. Employees are required to wash their hands at specified times, to wear hats or nets over their hair, and to wear special clothing.

The management of food safety falls under a set of rules generally known as Good Manufacturing Practice. Good Manufacturing Practice incorporates the regulations established by local, state, and federal officials, but usually is more detailed in specifying the particular practices of a firm. The practices are explicitly set forth in company documents, which include the firm’s safety goals, measurements to determine if the goals are being met, and controls put in place to ensure the safety of food.

Hazard Analysis Critical Control Point, first instituted in 1997 by the FDA’s Center for Food Safety and Applied Nutrition, is a more recent approach to safety improvement. Hazard analysis consists of identifying potential hazards and the points at which those hazards can be effectively controlled. An investigation of the 1994 salmonella ice cream outbreak, for example, identified the tanker trucks as a critical point for controlling viral and bacterial poisoning. The analysts recommended that ingredients for ice cream be hauled in dedicated tankers, that the tanks and seals be checked at regular intervals for cracks or leaks, and that the inspections be documented and monitored by responsible managers. The company also identified another control point, at which the ice cream was ready to ship, and began inspecting finished ice cream for microorganisms. Had Hazard Analysis Critical Control Point been practiced before the outbreak, the poisonings would have been avoided.

Drug manufacturing, like food manufacturing, is concentrated among large firms. The four largest drug firms produce 62 percent of the drug output of the United States, as measured by revenues. One reason for concentration is the large expenditure needed to bring a drug to market. In the year 2000, it cost $400 million on average to research and develop a successful drug and another $400 million to bring it to market. Much of the money is spent screening drugs that do not succeed; only about 1 in 5,000 probed chemicals makes it to market. Successful drugs go through long and complicated processes to meet regulatory requirements. It takes more than 8 years for the average drug to meet regulatory approval.

Regulators

In the United States, government regulation of food and drugs is a patchwork of overlapping laws and authority that reflects the division of powers and the diversity of contending interests within the American system. Local governments—city, county, and state—establish safety regulations for restaurants, water supplies, and sewage systems. Local inspectors visit restaurants and issue citations or close those that violate safety codes. Local governments usually own the facilities that provide mass water and sewage services to communities, and they regulate the drilling and inspection of private wells and septic tanks. State governments usually regulate establishments, other than restaurants, that manufacture, store, and sell food at retail, although city and county governments sometimes perform this function. The U.S. Congress establishes regulations for food and drugs involved in interstate commerce. The FDA sets the rules for accurate labeling of foods, which are enforced by a number of agencies. The Department of Agriculture inspects eggs, grains, meat, and poultry. The FDA inspects other foods for chemical and biological agents. The Centers for Disease Control and Prevention investigate outbreaks of food poisoning, and the Environmental Protection Agency enforces pesticide regulations. (Both the FDA and Centers for Disease Control and Prevention are part of the Department of Health and Human Services.)

The budgets devoted to inspections and enforcement are substantial. For 2004, Congress budgeted $797 million to the Food Safety and Inspection Service of the Department of Agriculture to inspect meat, poultry, and eggs. The Animal and Plant Health Inspection Service, which looks for diseases before they
enter the food supply, received a budget of $695 million for 2004. The FDA budget for 2004 was $1.7 billion.

The regulation of drugs falls to the FDA, which sets labeling rules and determines which drugs may be offered as over-the-counter medicines or as prescription-only from physicians. The FDA has long and costly procedures for approving new drugs for sale. Typically, a drug firm employs chemists, toxicologists, molecular biologists, statisticians, and computer modelers to scan the scientific literature for substances it hopes will be effective in treating a malady. Once the researchers identify or develop a substance, it is tested in vitro, that is, in an artificial environment such as a test tube, and in vivo, in laboratory animals such as mice. In these tests, researchers try to infer how the drug will influence the human body and how the body will influence the drug. Dosage, toxicity, absorption into the bloodstream, and effectiveness are of particular interest in these early studies.

Most potential drugs do not pass these first tests, but if a substance shows promise, it then moves to clinical trials, that is, testing in human subjects. These trials are conducted in specialized clinics (AIDS clinics, for example), in research hospitals, or sometimes in doctors' offices. To be approved, a drug must pass through three phases of clinical trials. In the first phase, healthy volunteers are subjected to a new drug, mainly to test for effectiveness and harmful effects. Subjects must be informed of the risks, and institutional review boards of competent professionals must approve the testing processes. The FDA may stop testing at any point in the process if it deems the drug too risky.

If a drug shows promise in the first phase, it moves into phase-two trials, which are conducted on patients. These trials use a small number of patients, not more than a few hundred, and are controlled—meaning that the treated patients are compared with a similar group that is not treated. The trials are closely monitored for effectiveness and safety. Only if a drug shows promise for effective treatment without harmful side effects does it move into phase three. In the third phase, the drug is usually tested in a few thousand patients to weigh the benefits against the risks to a general population.

If the benefits-to-risk ratio is acceptable, the testing firm applies to the FDA to approve the drug for sale either through prescription or over the counter. The FDA estimates that on average it takes 7 years to complete clinical trials and only about 20 percent of the drugs that enter clinical trials are approved. It takes another 18 months for the agency to review the application and approve a new drug.

Testing continues even after the drug is on the market. Phase-four trials study the long-term effects of drugs. If the long-term effects are sufficiently harmful, a drug will be taken from the market. Vioxx, a popular medication for arthritis, was removed from the market in late 2004 after it was discovered that long-term use could damage the heart.

Comprehensive testing provides additional knowledge about drugs, but also increases their cost and decreases their availability. U.S. tests are generally more stringent than their European counterparts, which means that many new drugs become available in Europe before they do in the United States. There is an inevitable tradeoff in the length and thoroughness of testing and the drugs' cost and availability. An agency that is very cautious about introducing only the safest drugs can damage the public health by holding valuable drugs off the market for too long. National regulation also sets a single standard for risk that all must accept, despite varying circumstances and individual tolerance for risk. A dying cancer patient may be willing to accept a great deal of risk in trying a new drug, whereas a healthy young adult may be willing to accept very little risk in taking a tranquilizer. In any case, complete knowledge about the undesirable effects of drugs, especially long-term effects, is unobtainable. For example, phenothiazine tranquilizers, approved for use by the FDA in the 1950s, had been in use for a decade before clinical reports of retinal degeneration appeared. The complexity of and variations in human biochemistry make it impossible to foresee all the potential effects of drug use.

Regulation of foods and drugs is increasingly international in scope. The World Trade Organization (WTO), established in December 1994, laid down rules governing food standards for international trade. The WTO's Sanitary and Phytosanitary Provisions represent an effort to harmonize national regulations and make all food regulations transparent. Among the WTO's goals is to promote trade in food and drugs without compromising their safety—no easy task. The United States, for example, permits the production and sale of genetically modified foods because the consensus of scientific opinion regards these foods as safe. The European Union (EU), however, does not permit their import because most Europeans think they are unsafe. U.S. firms claim this is an unfair restriction on trade, since scientific evi-
dence does not support the EU policy. Although a dispute resolution body has ruled in favor of the United States, the EU is contesting the ruling. The result is a trade dispute that will eventually be settled through the rules and procedures of the WTO, although most experts expect the United States to win. Regardless of who prevails, the more important point is that international bodies are becoming increasingly involved in setting safety standards that were once the domain of national governments.

Drugs developed in the United States and Europe are often reproduced in poorer countries without the consent of the companies that developed the drugs. This enables governments or companies in poorer countries to sell the drugs more cheaply or even give them away. For example, Brazilian firms manufacture AIDS drugs, which the government distributes free of charge to fight the spread of that disease. Although the program has succeeded in slowing the spread of AIDS, the large pharmaceutical companies that developed the drugs claim it is unsafe. This dispute will also be settled by the WTO or through international negotiations. As of early 2005, the dispute had not been resolved. Brazil still refuses to pay what American drug companies are asking, but has offered to pay a much lower licensing fee—which it is allowed to do under WTO rules. Experts say it may take some time for the dispute to be resolved. Regardless of what happens, because so many foods and drugs are traded across borders, international rules and regulations are gaining in importance.

CONCLUSION

In the sweep of human history, much progress has been made in the fight against foodborne diseases and the search for safe and efficacious drugs. In the economically developed countries, typhoid fever, botulism, chronic infections, and deficiency diseases such as pellagra are much less prevalent today than they were as recently as the nineteenth century. Many other diseases that are not food related—smallpox, polio, pneumonia, tuberculosis, malaria, hookworm, gangrene, to name a few—have also been eliminated or substantially reduced thanks to the development of drugs. The credit for this progress goes to science, technology, education, economic progress, and the practice of good hygiene. Despite the progress in improving the chances for a long and healthy life in the industrial world, there is no room for complacency toward food and drug safety.

A striking aspect of foodborne disease in the world today is the emergence of new pathogens responsible for outbreaks. In the 1950s, four bacteria—Staphylococcus aureus, Salmonella, Clostridium botulinum types A and B, and Shigella—were the main foodborne pathogens in the United States. In the 1960s, Vibrio cholerae non-01, Clostridium botulinum type E, and hepatitis A were added to the list. In the 1970s, confirmed outbreaks were caused by Vibrio parahaemolyticus, Vibrio cholerae 01, E. coli, Campylobacter jejuni, and Vibrio vulnificus. In the 1980s, Listeria monocytogenes, new strains of E. coli, Salmonella enteritidis, and Norwalk viruses caused outbreaks. The discovery of new pathogenic diseases is partly due to improved detection methods, but increased travel, changes in eating habits (eating out), new production methods (raising sedentary chickens), and the remarkable ability of pathogens to adapt (as demonstrated by the HIV and SARS viruses) are also factors. Adaptability of microorganisms means the fight against foodborne pathogens will be a long-running war with no final victory.

Genetically modified food is another area of concern today. Although the transfer of genetic material from one organism to another occurs naturally in evolution, cross-breeding and especially recombining genes in the laboratory has sped the process along. The danger is that the new genes will produce toxins when combined with existing genes. So far this danger has not materialized, but only continued vigilance will keep it in check. Biotech companies and regulatory bodies carefully monitor all genetically modified foods for toxins, allergens, and other dangers.

The main areas of concern with drugs are their expense, their failure at times to cure the intended illnesses or combat the symptoms, and their side effects. As already mentioned, false leads—the many attempts at producing new drugs that fail—and stringent regulations drive up the costs of drugs. In the United States, drugs are often out of the reach of ordinary citizens without health insurance, and those with insurance are finding their premiums ever more expensive, thanks in part to rising drug prices. Insurance companies, policymakers, and others are looking for ways to lower these prices without slowing research and innovation.

Despite huge amounts of money spent on drug research and the undeniable achievements of drugs in fighting diseases, results have been disappointing in some areas. For example, many types of cancer
have been stubbornly resistant to drugs. The National Cancer Society estimates that, as of the early 2000s, roughly 1.3 million Americans are diagnosed annually, and between 500,000 and 600,000 die. Finally, despite the close scrutiny drugs receive from regulators, they still cause many serious side effects. One study estimated that in U.S. hospitals, 100,000 patients die each year from adverse reactions to drugs. Adverse reactions also cause serious illness, for which the prescription is often more drugs.

Food and drug safety is an even more critical problem in the developing world. Many diseases that are minor in the developed world wreak havoc in poor countries. Each year about 17 million persons, nearly all from developing countries, contract typhoid fever, mainly from contaminated food and water. Of these, about 1 million die. Cholera, another disease spread through contaminated food and water, has swept through the developing world in a wave of epidemics. One epidemic that started in Indonesia in the 1960s spread through East Asia, India, the Soviet Union, and Iran. In 1970 cholera reached West Africa, where the disease had not been experienced for 100 years and resistance was low, resulting in a high death toll. In 1991 the epidemic struck South America, then returned to India and Pakistan in 1992, via a slightly altered bacterium.

Malaria has been all but eliminated from the industrial countries, but in the developing world 300 million cases of malaria and more than a million deaths occur each year. Ninety percent of the deaths occur in sub-Saharan Africa, mainly among children. The reason for the high death rate is primarily economic. Poor populations cannot afford the insecticides and drugs that would control the disease. The economic problem is compounded by the evolution of mosquitoes and parasites resistant to existing treatment. Likewise AIDS, whose incidence and mortality rates are declining in industrial countries, is raging in Africa. Of the nearly 3 million deaths caused by AIDS in 2003, over two-thirds were in Africa. Poverty, ignorance of the disease, and lack of affordable medicine are the main reasons Africans have not combated AIDS successfully.

Foods and drugs will never be perfectly safe, but there is reason to be optimistic that they will become safer for more people. The greatest gains are to be had among the poorer countries of the world, where technology and hygienic practices of the developed world can be gradually applied. In the richer countries, advancing science and economic progress can be expected to produce yet more effective methods of controlling pathogens and toxins.

Jack High

REFERENCES


Glossary

Bacteria. The plural of bacterium, a one-celled organism that has no chlorophyll and multiplies by simple division. Bacteria assume three main shapes—spherical (cocci), rodlike (bacilli), and spiral (spirilla). Bacteria are responsible for many diseases, including Lyme disease, pneumonia, tuberculosis, and syphilis.

Botulism. A paralytic disease caused by toxins of Clostridium botulinum. The poisoning results mainly from improper home canning and can be fatal even in small doses.

Bovine spongiform encephalopathy (BSE). Popularly known as mad cow disease, BSE is caused by a virus similar to that which causes scrapie in sheep. BSE may be transmissible to humans through food in the form of Creutzfeld-Jakob disease, a deadly brain infection.

Campylobacteriosis. An infection of the intestinal tract caused by Campylobacter coli and Campylobacter jejuni, bacteria transmitted to humans through meat and poultry. It is the most common cause of infective diarrhea in developed countries.

Cholera. An acute bacterial infection caused by Vibrio cholerae, transmitted through food and water, and characterized by diarrhea, vomiting, and delirium.

Coliform. Shortened form of coliform bacillus, a rod-shaped bacterium found in the colon and fecal matter. A high coliform count in water means that it is unsafe to drink. An acceptable coliform count is 500 per hundred milliliters; the Ganges River in India has a coliform count of more than 150 million per hundred milliliters.

Drug. Any substance used as a medicine or an ingredient in a medicine.

Food. Any substance taken in by a plant or animal that enables it to live and grow. In this broad definition, water is considered a food; a narrower definition distinguishes solid food from drink.

Genetic engineering. The intentional alteration of genes or transfer of genes from one organism to another. Genetic engineering is commonly used to produce pest-resistant crops for humans and other animals. It is also used to alter the nutritional characteristics of crops, as in golden rice, which is rice that contains beta-carotene (vitamin A).

Mad cow disease. See Bovine spongiform encephalopathy (BSE).

Pellagra. A disease caused by a deficiency of niacin (vitamin B6) and characterized by diarrhea, dermatitis, dementia, and, if not treated, death. Associated with a maize diet. With mortality rates of 70 percent, the disease caused widespread misery and death in Europe and America between 1730 and 1930.

Poison. A substance that causes illness or death when taken in small quantities.

Salmonellosis. A disease caused by any of the Salmonella bacteria. It is usually transmitted through eggs and meat that have been inadequately cooked. Characterized by vomiting and diarrhea and is generally self-limiting.

Scurvy. A chronic disease caused by lack of ascorbic acid (vitamin C) and characterized by weakness, anemia, and bleeding from the mucous membranes.

Typhoid fever. A disease caused by Salmonella typhi, a bac-
terium that spreads from human to human through contaminated water or food. The disease is endemic in countries such as India, with poor facilities for sanitation.

**Vaccination.** The introduction of dead bacteria into the body to produce immunity to a disease. Edward Jenner used cowpox to vaccinate against smallpox.

**Virus.** An extremely small organism, or protein, that causes disease. Smallpox and various strains of influenza are caused by viruses.

**Vitamin.** Any of various complex organic compounds necessary to the healthy functioning of the body but which the body does not produce in sufficient quantities to maintain health. Vitamins must be obtained from foods or supplements.

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**DOCUMENTS**

**Document 1. Excerpts from the Pure Food and Drugs Act, 1906**

Numerous food and drug safety bills were introduced into Congress in the early 1900s, but all were defeated by industry lobbyists. Then, in 1906, muckraking journalist Upton Sinclair published his best-selling novel, *The Jungle*, exposing the poor hygienic conditions in the nation's meatpacking industry. The uproar over the book goaded Congress into finally passing the *Pure Food and Drugs Act* in 1906. Along with the *Meat Inspection Act* of the same year, the legislation enacted the nation's first systematic federal regulations of food and drug safety.

**PURE FOOD AND DRUGS ACT OF 1906**

**AN ACT** for preventing the manufacture, sale, or transportation of adulterated or misbranded or poisonous or deleterious foods, drugs, medicines, and liquors, and for regulating traffic therein, and for other purposes.

*Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled,*

**SEC. 1. MANUFACTURE OF ADULTERATED FOODS OR DRUGS.**

That it shall be unlawful for any person to manufacture within any Territory or the District of Columbia any article of food or drug which is adulterated or misbranded, within the meaning of this Act;

**SEC. 2. INTERSTATE COMMERCE OF ADULTERATED GOODS.**

That the introduction into any State or Territory or the District of Columbia from any other State or Territory or the District of Columbia, or from any foreign country, or shipment to any foreign country of any article of food or drugs which is adulterated or misbranded, within the meaning of this Act, is hereby prohibited.

**SEC. 4. CHEMICAL EXAMINATIONS.**

That the examinations of specimens of foods and drugs shall be made in the Bureau of Chemistry of the Department of Agriculture, or under the direction and supervision of such Bureau, for the purpose of determining from such examinations whether such articles are adulterated or misbranded within the meaning of this Act.

**SEC. 6. DEFINITIONS.**

That the term "drug," as used in this Act, shall include all medicines and preparations recognized in the United States Pharmacopoeia or National Formulary for internal or external use, and any substance or mixture of substances intended to be used for the cure, mitigation, or prevention of disease of either man or other animals. The term "food," as used herein, shall include all articles used for food, drink, confectionery, or condiment by man or other animals, whether simple, mixed, or compound.

**SEC. 7. ADULTERATIONS.**

That for the purposes of this Act an article Shall be deemed to be adulterated:

**IN CASE OF DRUGS:**

FIRST. If, when a drug is sold under or by a name recognized in the United States Pharmacopoeia or National Formulary, it differs from the standard of strength, quality, or purity, as determined by the test laid down in the United States Pharmacopoeia or National Formulary official at the time of investigation.

SECOND. If its strength or purity fall below the professed standard or quality under which it is sold.

**IN THE CASE OF FOOD:**

FIRST. If any substance has been mixed and packed with it so as to reduce or lower or injuriously affect its quality or strength.

SECOND. If any substance has been substituted wholly or in part for the article.

**SEC. 8. MISBRANDING.**

That the term "misbranded," as used herein, shall apply to all drugs, or articles of food, or articles which enter into the composition of food, the package or label of which
shall bear any statement, design, or device regarding such article, or the ingredients or substances contained therein which shall be false or misleading in any particular, and to any food or drug product which is falsely branded as to the State, Territory, or country in which it is manufactured or produced.

SEC. 13. EFFECTIVE DATE.
That this Act shall be in force and effect from and after the first day of January, nineteen hundred and seven.

 APPROVED, JUNE 30, 1906.


In 1995, the World Trade Organization adopted a measure on food safety called the WTO Agreement on the Application of Sanitary and Phytosanitary Measures (SPS Agreement). The accord was an attempt to prevent national food regulation from hindering international trade. In May 2003, the United States complained to the dispute settlement body that the European Union’s refusal to admit genetically modified foods into EU nations violated the SPS Agreement.

Members,

Reaffirming that no Member should be prevented from adopting or enforcing measures necessary to protect human, animal or plant life or health, subject to the requirement that these measures are not applied in a manner which would constitute a means of arbitrary or unjustifiable discrimination between Members where the same conditions prevail or a disguised restriction on international trade;

Desiring to improve the human health, animal health and phytosanitary situation in all Members;

Noting that sanitary and phytosanitary measures are often applied on the basis of bilateral agreements or protocols;

Desiring the establishment of a multilateral framework of rules and disciplines to guide the development, adoption and enforcement of sanitary and phytosanitary measures in order to minimize their negative effects on trade;

Recognizing the important contribution that international standards, guidelines and recommendations can make in this regard;

Desiring to further the use of harmonized sanitary and phytosanitary measures between Members, on the basis of international standards, guidelines and recommendations developed by the relevant international organizations, including the Codex Alimentarius Commission, the International Office of Epizootics, and the relevant international and regional organizations operating within the framework of the International Plant Protection Convention, without requiring Members to change their appropriate level of protection of human, animal or plant life or health;

Recognizing that developing country Members may encounter special difficulties in complying with the sanitary or phytosanitary measures of importing Members, and as a consequence in access to markets, and also in the formulation and application of sanitary or phytosanitary measures in their own territories, and desiring to assist them in their endeavours in this regard;

Desiring therefore to elaborate rules for the application of the provisions of GATT 1994 which relate to the use of sanitary or phytosanitary measures, in particular the provisions of Article XX(b) (1);

Hereby agree as follows:

Article 1: General Provisions
1. This Agreement applies to all sanitary and phytosanitary measures which may, directly or indirectly, affect international trade. Such measures shall be developed and applied in accordance with the provisions of this Agreement.

Article 2: Basic Rights and Obligations
2. Members shall ensure that their sanitary and phytosanitary measures do not arbitrarily or unjustifiably discriminate between Members where identical or similar conditions prevail, including between their own territory and that of other Members. Sanitary and phytosanitary measures shall not be applied in a manner which would constitute a disguised restriction on international trade.

Article 3: Harmonization
1. To harmonize sanitary and phytosanitary measures on as wide a basis as possible, Members shall base their sanitary or phytosanitary measures on international standards, guidelines or recommendations.

Article 4: Equivalence
1. Members shall accept the sanitary or phytosanitary measures of other Members as equivalent, even if these measures differ from their own or from those used by other Members trading in the same product, if the exporting Member objectively demonstrates to the importing Member that its measures achieve the importing Member’s appropriate level of sanitary or phytosanitary protection. For this purpose, reasonable access shall be given, upon request, to the importing Member for inspection, testing and other relevant procedures.
Article 5: Assessment of Risk
1. Members shall ensure that their sanitary or phytosanitary measures are based on an assessment, as appropriate to the circumstances, of the risks to human, animal or plant life or health, taking into account risk assessment techniques developed by the relevant international organizations.

2. In the assessment of risks, Members shall take into account available scientific evidence; relevant processes and production methods; relevant inspection, sampling and testing methods; prevalence of specific diseases or pests; existence of pest—or disease—free areas; relevant ecological and environmental conditions; and quarantine or other treatment.

Article 11: Consultations and Dispute Settlement
2. In a dispute under this Agreement involving scientific or technical issues, a panel should seek advice from experts chosen by the panel in consultation with the parties to the dispute. To this end, the panel may, when it deems it appropriate, establish an advisory technical experts group, or consult the relevant international organizations, at the request of either party to the dispute or on its own initiative.

Source: World Trade Organization.