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Food Chemistry and U.S. Food Regulations

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The Agriculture and Food Chemistry Division (AGFD) was founded in 1908 shortly after passage of the first U.S. food regulations in 1906. Modern food regulations started with the passage of the Food Drug and Cosmetic Act in 1938. This Act has been amended several times to keep pace with developments in food chemistry. In 1958 the Food Additives Amendment was enacted to control substances added to food. Since 1958 scientific techniques have been developed to evaluate the safety and carcinogenicity of substances in the food supply. In the 1970s and 1980s AGFD symposia and books addressed compounds of concern in foods. In the 1990s food safety and nutrition regulations followed new developments in food and nutrition chemistry. Recently, the well-studied toxin acrylamide was discovered in food and presented regulators with new questions on safety and control in the food supply. Discoveries and developments in chemistry such as those in nanotechnology will continue to present challenges to food regulators.

KEYWORDS: Food chemistry; food regulation; food history; FDA food regulations; nutrition

INTRODUCTION

Throughout history, people and governments have sought to control and regulate dietary intake. This may have been because of dietary religious laws, concerns about food safety, or food economic adulteration. With the advent of modern chemistry, food regulations have followed advances in the understanding of food chemistry. This paper will attempt to highlight significant food chemical advances and show how they influenced food regulation.

Perhaps the earliest recorded regulations by a recognized authority are in the *Bible*. Adam and Eve were prohibited by God from eating forbidden fruit. As a result of their eating a forbidden apple, they were cast out of the Garden of Eden, causing mankind unhappiness and sorrow for all time (*1*).

King Hammurabi (*2*) of ancient Babylon, who ruled from 1795 to 1750 B.C.E., is often credited with giving the world's first written code of laws. In his laws he took great care to see that provisions were made with regard to pricing of beer. The laws stated that sellers must give fair measure of beer for grain. Failure of the seller to give an appropriate amount of beer for money tendered resulted in severe penalties such as death by drowning if convicted. Since that time there have been many ancient laws regarding purity of beer and wine.

There are many possible references to food safety in the *Bible*. The dietary laws of Moses could have come about to prohibit the consumption of scavenged or diseased animals. These may have been as a result of observing a pattern of consumption of these animals that then resulted in sickness or death.

The early Chinese also had concerns about food safety. Chinese medicine has a long history of foods that prevented or cured disease. Confucius (*3*) was one of the first to warn about eating spoiled or contaminated food. Later, many of these Confucian prohibitions were incorporated into early Chinese food safety regulations.

It seems that fraud and adulteration of food were widespread during ancient times. Because of the importance of the food trade to the Roman Empire, Roman civil law included edicts against any kind of commercial fraud or contamination of food. For example, the Romans had laws against watering of wine or improvement of wine by adding various sweeteners. However, at that time there were few ways of detecting adulteration, and therefore the practice could and did become widespread. Pliny the Elder (*4*) deplored merchants who "spoil everything with greed and adulterations". Pliny was one of the first advocates of simple food, not unlike the raw and natural food advocates of today.

The practice of adulteration of food and particularly that food associated with commerce continued on into the early Middle Ages (*3*). Laws against food adulteration and fraud may have been decreed by early kings, but with the passing of time, these were often forgotten or unenforced. Certainly the turmoil of the period and the absence of any central, long-lasting civil authority made it impossible to sustain any law.

Still, certain countries did pass laws regarding food and wine in the Middle Ages. In 1266 the English Parliament enacted the Assize of Bread (*5*), which prohibited the sale of any staple food product that is not wholesome. This was perhaps the most comprehensive law ever enacted to address food safety. In 1516 the provincial capital of Bavaria proclaimed the pure beer law or Reinheitsgebot (*6*). This law stated that the only ingredients of beer must be barley, hops, and water (they did not know about yeast as such). They did know that there was a substance called "Godisgood" in the fermentation cake, which worked the magic of converting the grain mash to alcohol.

BEGINNINGS OF FOOD CHEMISTRY AND ITS IMPACT ON FOOD REGULATIONS

The only way ancients had of analyzing food was by organoleptic means, which is by use of the senses of smell, taste, sight,

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Table 1. Food Adulterants Identified by Frederick Accum

food	adulterant
red cheese	colored with red lead and mercury sulfide
cayenne pepper	colored with red lead
pickles	colored green with copper salts
vinegar	sharpened with sulfuric acid and contained tin and lead
confectionery	red sweets colored with red lead and mercury sulfide
	green sweets contained copper salts including arsenate
olive oil	lead from presses

and touch. Even by these crude methods some foods were discovered and recognized as being unfit to eat or unsafe. Lavoisier (*7*) was one of the first to realize that life is a chemical function and that food was the fuel of the body. The methods of organic analysis as devised by Liebig (*8*) resulted in the growth of organic chemistry and tools needed for the development of food chemistry. The earliest quantitative analyses of food materials recorded were made by Pearson in 1795 (*9*). Pearson estimated that portions of water, starch, fibrous matter, extracted materials, and ash were constituents of food (potatoes). He also recognized the presence of fats, acid, and sugar.

In the early 1800s a German chemist by the name of Frederick Accum (*10*) was the first to discover food adulteration by using established chemical analyses. Coffee and tea were popular imports in England at the time and, being very expensive, were popular foods to counterfeit. Beer, wine, milk, and candy, although not as expensive, were also popular targets for adulteration. Through his analyses Accum recognized the presence of lead and copper salts in many commodities. He also discovered that starch in rice powder and wheat flour were often used to thicken cream. The bright colors used to attract children to candy often contained copper, lead, and mercury salts. Other food adulterations identified by Accum are listed in **Table 1**.

Accum had become aware of many problems through his analytical work and decided to publish a treatise on the adulterations of food. This book was revolutionary in that it identified not only adulterations but the methods of detecting them. In fact, the sale of such poisons was illegal under an act of Parliament passed during the reign of George III. However, there were no reliable tests for these poisons, so the law was not rigorously applied and few offenders were caught. In the preface to his book, Accum remarked that the art of counterfeiting and adulteration had developed in England to such an extent that spurious articles of all kinds could be found everywhere. The book sold out within a year. It was also translated from German to English and sold in America, where it undoubtedly influenced the American public. He regarded the adulteration of food and drink as a criminal offense. The use of poisonous coloring matters to manufacture jellies and sweets that were used to attract children was particularly offensive. Accum was so enraged that he published the names and addresses of traders convicted by the courts of adulterating food and drink with poisonous additives. This made powerful enemies, who finally succeeded in getting him charged with mutilating books (probably unfairly) in the library of the Royal Institution. Unwilling to face public disgrace, he fled back to Germany in 1821. Unfortunately for the public, Accum's work was largely disregarded, and unsafe culinary practices thrived for the next 30 years.

In 1850 Arthur Hassall (*11*) succeeded in showing that some samples of coffee purchased in London were adulterated with chicory. His analysis was performed by simple microscopic examination. The work reported in several London newspapers earned him the title of Chief of the Analytical Sanitary Commission. Between 1851 and 1854 Hassall analyzed 2500 food samples and published the results in the *Lancet*. He examined samples first by microscope and then by chemical analysis. He then threatened to publish the names of vendors who sold adulterated samples. Just as Accum, Hassall found that lead and mercury compounds were in cayenne pepper and that copper salts were found in bottled fruits and pickles. And just as Accum had claimed, he found that confections were contaminated with toxic salts. Hassall was the first to keep meticulous records about where and when the food samples were purchased and carefully showed that adulterated articles were sold as genuine. He set a fine example for the many food regulatory chemists who were to follow.

The first food adulteration act in England was passed in 1860 (*10*) following Hassall's work. In 1872 the act was revised and made provision for the appointment of public analysts. In 1874 the Society of Public Analysts was founded with Hassall as its first president. A report of Hassall and a select committee provided the basis for the Sale of Food and Drugs Act of 1875. The scientific investigations and subsequent laws provide the foundation for future food regulations in the United States and around the world.

DEVELOPMENT OF FOOD CHEMISTRY AND REGULATIONS IN THE UNITED STATES

Although early American chemists were probably aware of Accum and Hassall's works, most investigations involved analyses on the composition of feeds and foodstuffs. A foundation for chemistry and food regulations started when President Lincoln appointed the chemist Charles M. Wetherill to serve in the new Department of Agriculture for the United States (USDA) (*12*). This was the beginning of the Bureau of Chemistry, which was the predecessor of the Food and Drug Administration. In 1880 Peter Collier, Chief Chemist of the U.S. Department of Agriculture, recommended passage of a national food and drug law after conducting his own food adulteration investigations. Although this bill did not pass, it was the beginning of a national recognition of the need of laws to prevent food adulteration. In 1883 Dr. Harvey W. Wiley (*13*) became Chief Chemist and expanded the Bureau of Chemistry's food adulteration studies. In 1898 the Association of Official Agricultural Chemists established the committee on food standards headed by Dr. Wiley. Dr. Wiley began to incorporate these food standards into USDA food statutes. To bring his cause to the public, in 1902 he organized a volunteer group of healthy young men, called the Poison Squad, who tested the effects of chemicals and adulterated foods on themselves. His continued campaign (*14*) for a pure food and drug act resulted in the Food and Drug Act that eventually would be passed in 1906 and signed by President Theodore Roosevelt. Passage of the Act followed shocking disclosures of the unsanitary conditions in meatpacking plants, the use of poisonous preservatives and dyes in foods, and cure-all claims for worthless and dangerous patent medicines. The Act prohibited interstate commerce in misbranded and adulterated foods, drinks, and drugs. Subsequently, in 1907, the first Certified Color Regulations, requested by manufacturers and users, listed seven colors found suitable for use in foods.

Although the American Chemical Society (ACS) was founded in 1876, there was no organized effort to group food chemistry papers into topical sections until 1904 (*15*). The Agricultural Sanitary and Physiologic Chemistry section was renamed the Agricultural and Food section, which went on to become the Agricultural and Food Chemistry Division (AGFD) in 1908. The first paper presented in the newly organized division was on the subject of whiskey.

Table 2. Analytical Methods Available by 1938

analysis	years method developed
physical, refractometry, colorimetry, spectrometry, electrometric, vicosimeter freezing point, surface tension	1920−1937
coloring substances	1916−1937
preservatives	1916−1937
metals	1924−1936
milk analysis	1918−1936
milk products analysis	1925−1935
oils and fats	1922−1936
sugar foods and carbohydrates	1912−1935
gums, cereals, starches, polysaccharides, fruits, jellies and jams, vegetable products	1926−1935
spices, flavors, condiments	1920−1935
alcoholic beverages	1919−1934
meat, meat products, fish, eggs	1920−1935
vitamins	1935−1937
inorganic compounds	1928−1937

Even before the founding of the ACS, American chemists visited Liebig's laboratory in Germany for agricultural chemistry training. Scientists in the division began to concentrate on unidentified growth factors that perplexed food chemists during that period. Liebig classified food constituents as proteins, carbohydrates, fats, and minerals. Professor E. V. McCollum of the University of Wisconsin and a member of the Agriculture and Food Chemistry Division established the first rat colony for experimental nutritional studies. This pioneering approach became a major tool for the discovery and understanding of the growth factors that were to become so important in agricultural production as well as the prevention of disease in humans. Studies at this time delved into the more complex structures of food components and their effect on human physiology. The Division of Agricultural and Food Chemistry has maintained its close association with the USDA over time (*15*).

By 1930 the Bureau of Chemistry and the Agricultural and Food Chemistry Division were stretched into many interests. Therefore, the Bureau of Chemistry was reorganized into two divisions; one, the Food Drug Insecticide Administration with a regulatory focus, later shortened to FDA, and the other, the Bureau of Chemistry and Soils, with primarily a research focus. By 1938, the focus on food and food chemistry in conjunction with advances in general chemistry produced analytical methods for many common foodstuffs. **Table 2** lists analytical methods cited by Jacobs in 1938 (*16*) and which were then available for the analysis of foods. The availability of these methods enabled detection of adulteration in food products and highlighted the need for more detailed food regulations.

As food chemistry progressed, regulations followed suit. In 1930, the McNary−Mapes Amendment authorized FDA to regulate "standards of quality and fill" for canned food, excluding meat and milk products. Due to the advances in food chemistry, in 1933 FDA recommended the complete revision of the obsolete 1906 Food and Drugs Act. After five years of deliberation, the Federal Food Drug and Cosmetic Act of 1938 (*12*) was passed by Congress. New provisions included (1) providing that safe tolerances be the set for unavoidable poisonous substances; (2) authorizing standards of identity, quality, and fill of containers for foods; (3) authorizing factory inspections: and (4) adding the remedy of court injunctions to the previous penalties of seizures and prosecutions. In 1940 FDA was transferred from the Department of Agriculture to the Federal Security Agency (which later became the Department of Health Education and Welfare) (HEW) with Walter G. Campbell appointed as the first Commissioner of Food and Drugs. In 1949 the FDA published guidance to industry for the first time. This guidance, called "Procedure for the Appraisal of Safety in Foods, Drugs, & Cosmetics", became known as the "black book" (*17*).

MODERN ERA OF FOOD CHEMISTRY AND FOOD REGULATION

Although it has been amended many times, the Food Drug and Cosmetic Act of 1938 remains the basic statute governing food regulation in the United States. A major difference between this act and the 1906 act was the focus on food safety. There were food safety concerns about the increasing use of insecticide sprays and concerns over chronic ingestion of lead and arsenic residues left over on fruits and vegetables after harvesting. In addition to short-term toxicity testing, the need for longer-term chronic tests became evident. A 1949 FDA monograph (*17*) gave procedures for the appraisal of the safety of chemicals in foods, drugs, and cosmetics and mandated the performance of chronic tests on substances added to food. To make matters more complex, both chemical and toxicological measurements were becoming much more sensitive and indicated more compounds might be carcinogenic. Concerns were also growing about long-term consumption of these compounds, so that in 1958 the Food Additives Amendment (*18*) required manufacturers of new food additives to establish safety. It also contained the Delaney amendment that prohibited the approval of any food additive shown to induce cancer in humans or animals. Carcinogen testing became so sensitive that it became unclear whether a substance was truly a carcinogen in the amounts at which it was normally consumed. In response, in 1959 FDA published another monograph (*19*) that contained a separate section on carcinogen testing, sections on dietary factors, the proper number of animals, the evaluation of malignancy, and other scientific issues to be considered in carcinogen tests.

By 1970 toxicity tests were becoming so complicated and difficult to interpret that they were nearly useless. Chemists exacerbated the situation by driving down detection limits for some suspected carcinogens to parts per billion or parts per trillion levels. In an effort to address this situation, the FDA developed a statistical risk assessment method, which was first applied in the sensitivity of method regulations in 1973. In the 1970s there was also the development of the National Cancer Institute cancer bioassay program, which eventually led to the development of the National Toxicology Program (NTP) bioassay program in which FDA plays an integral part today (*20*). In 1982 FDA published the first Redbook and has continuously revised it over the years (*21*); this successor to the 1949 "black book" was officially known as "Toxicological Principles for the Safety Assessment of Direct Food Additives and Color Additives used in Food". Since then there have been several modifications

to this risk assessment; however, the problems then plaguing researchers continue today (*22*). Clearly, as Dr. Wiley noted, animals, and not humans, need to be used as the test animals for toxicity testing. But experience and science have shown that the application of toxicity data obtained from rats does not necessarily apply to humans and that dietary exposure to many food chemicals is difficult to assess.

To estimate exposures to food chemicals the FDA initiated the Total Diet Study (*23*). This study involved analysis of a group of foods that reflect the average food consumption patterns of a given population. The results of these analyses can be used to estimate the average intake of chemical contaminants from eating these foods. Early studies in the 50s were concerned with radiochemical contamination of milk brought about by radioactive fallout from nuclear weapons testing. These analyses were so useful that the Total Diet Study was expanded to include many more foods and many more chemical contaminants. During the 1970s, FDA expanded the list of analytes to include pesticide residues, toxic elements, and industrial chemicals. Beginning in 1973, FDA broadened the scope to include nutrients as well as contaminants; by 1983, foods were analyzed for 11 nutrients. Vitamin B6 and folate were added by 1990. The use of the Total Diet Study by FDA has continued, and it is routinely used to monitor contaminants and nutrients in the U.S. food supply. More food groups, contaminants, and nutrients are currently being monitored (*23*).

FOOD CHEMISTRY, NUTRITION, TOXICANTS, AND REGULATION

Thus far, we have discussed the compounds in food in terms of chemicals added either intentionally or unintentionally. Major concerns about the food supply as identified by consumer surveys have been food additives, pesticide residues, food-processing aids, and preservatives. In the early 1980s the FDA started ranking food safety hazards (*24*) in descending priority as shown in **Table 3**.

Clearly this ranking was almost opposite to consumer concerns. This focus by the FDA served to de-emphasize food additives and emphasize nutrients and natural food components.

But by far the largest quantity of compounds in foods comes from the foods themselves, and advances in chemistry caused food scientists to realize their many challenges in food safety assessment. Early in history man discovered that not all natural compounds are innocuous and that some plants and animals or their products contain toxic compounds. A simple element of food processing such as cooking might render a noxious plant edible. This fact was known intuitively by early peoples but required the advent of modern chemistry to describe changes in chemical composition and nutrients. Innovation and technological advances in toxicology, the biomedical sciences, and pharmacology slowly changed our understanding of the relationships between these natural compounds and whether they have detrimental or positive effects on health. Throughout the 20th century there has been a growing awareness of changes in food compounds produced by processing and storage. With the urbanization of the U.S. population and the growing dependence on processed foods, the effect of food processing on our food supply became more and more important. In the 1970s food chemical safety research focus shifted away from food additives and contamination to food formulation and processing. The importance of food formulation and processing was highlighted by the inadvertent omission of chloride from soy-based infant formulas, causing the malnourishment of several infants (*25*). In 1980 the Infant Formula Act (*12*) established special FDA controls to ensure nutritional adequacy and safety. Studies on food constituents raised concern about naturally occurring or process-induced compounds. Chemists studied antinutritional or toxic components in foods following the discovery of compounds such as lysinoalanine in soy protein products. Scientific literature identified compounds from a variety of sources that have toxic or potentially toxic effects. Included in such compounds were protease and amylase inhibitors, lipid hydroperoxides, mutagens derived from tryptophan, mutagens in heated foods, lysinoalanine, D-amino acids, isopeptides, aflatoxins, vomitoxins, various alkaloids, and constituents of carrots and celery (*26*).

Table 3. Rank of Food Safety Hazards[a]

1. microbiological
2. nutritional
3. natural
4. environmental contaminants
5. pesticide residues
6. food additives

[a] Microbiological is greatest hazard.

From the 1970s onward very extensive investigations have also been done on the beneficial compounds in foods including classical nutrients in foods. By 1995, a partial list of these compounds would include vitamins, citrus phytochemicals, soy flavones and isoflavones, phenolic phytochemicals in wine, fruits, and tea, and organosulfur and organoselinium compounds in onion and garlic (*27*). Since then and up until the present time there have been extensive scientific studies on health-promoting constituents. The results of some of these studies are continually being reported in the popular press, which leads to the desire on the part of food manufacturers to include and advertise health-promoting compounds in their products.

It became clear that supplementation of the diet even with an essential amino acid such as tryptophan could have harmful effects. In 1989 (*28*) FDA issued a nationwide recall of over-the-counter dietary supplements containing 100 mg or more of L-tryptophan. Consumption of L-tryptophan tablets was associated with the U.S. outbreak of eosinophelia myalgia syndrome (EMS). By 1990 over 1500 cases of EMS including 38 deaths had been confirmed by the Centers for Disease Control and Prevention. FDA then prevented the importation of L-tryptophan. Intensive scientific investigations were done at that time by FDA to determine if the culprit was L-tryptophan or a reaction product of L-tryptophan produced during its manufacture. Some FDA scientists and independent researchers believed that the causative agents were reaction products of L-tryptophan.

In 1990 the Nutrition Labeling and Education Act (NLEA) (*12*) required all packaged foods to bear nutrition labeling. In addition, it required all health claims for foods to be consistent with terms defined by the Secretary of Health and Human Services. The law preempted all state requirements about food standards, nutrition labeling, and health claims and, for the first time, authorized some health claims for foods.

In response to the health claims that were being made on nutritional supplements, the Dietary Supplement Health and Education Act (*12*) was passed by Congress in 1994. This Act defined dietary supplements and dietary ingredients and classified them as food. It also established specific labeling requirements, provided a regulatory framework, and authorized FDA to promulgate good manufacturing practice regulations for dietary supplements.

FOOD CHEMICAL SAFETY AND HACCP

HACCP stands for Hazard Analysis and Critical Control Point system. This system was developed by the military and NASA. The Pillsbury Co. first used HACCP for the assurance of safety of

food intended for the U.S. Space program. In 1973 the FDA based mandatory regulation for low-acid canned foods on HACCP.

In 1989 the National Advisory Committee on Microbiological Criteria for Foods (NACMCF) encouraged many food companies to require their vendors and suppliers to develop HACCP systems. These systems shifted the emphasis from after-the-fact inspection and testing to systematic identification of potential hazards and planned prevention in the food manufacturing and distribution system. HACCP stimulated a new approach to food safety regulation by U.S. federal regulatory agencies. In response to the increasing number of foodborne outbreaks due to microbiological contamination in seafoods, FDA mandated the use of HACCP for control of microbial, chemical, and physical hazards in seafoods and seafood products (*29*). For chemical hazards HACCP required that manufacturers routinely monitor their food ingredient supplies and also take steps to prevent formation of toxins during food processing, packaging, and distribution. For a more complete description of how chemical hazards are treated in seafood HACCP, the reader is referred to the link on *Fish and Fishery Products Hazards and Control Guide* under Seafood HACCP (*29*). FDA recommended the use of HACCP systems in food production and later mandated their use in fruit juice production (*29*).

In 2003 the National Academy of Sciences released a report on the scientific criteria to ensure safe food commissioned by FDA and the Department of Agriculture. This report buttressed the value of the HACCP approach to food safety already in place in FDA. It said that there was a continued need to make food safety a vital part of our overall public health mission (*30*).

IMPACT OF 9/11 ON FOOD REGULATIONS

After the events of September 11, 2001, the Public Health Security and Bioterrorism Preparedness and Response Act of 2002 (*31*) was passed. Provisions of this Act included a requirement that FDA issue regulations to enhance controls over imported and domestically produced commodities that it regulates. This produced two major regulations by the FDA: the first, to register all food production facilities, and the second, to require importers of food to provide prior notification of the foods they intended to import. The ability of FDA to detain and seize food products in violation of these regulations was enhanced. Also, there was a requirement for record keeping such that in the event of a terrorist attack involving a food product, it could be traced from production or importation through the distribution chain to the consumer.

Through its own efforts and in collaboration with the industry, FDA attempted to do a risk assessment in terms of the toxic chemical agents that might be employed and appropriate foods a terrorist might target. FDA has also undertaken a research program to enhance this risk assessment and to assess the fate of potential toxic agents in foods. When possible and when the research findings are applicable to products for conventional food safety, this research has been published. These activities have put FDA on a much firmer footing in dealing with terrorists' attacks on the food supply. The 2004 Bioshield Act (*32*) authorized FDA to review procedures to enable rapid distribution of countermeasures to chemical, biological, and nuclear agents that might be used in a terrorist attack against the United States. For current activities on food defense the reader is referred to FDA's current Website on Food Defense (*33*).

DISCOVERIES OF LYSINOALANINE AND ACRYLAMIDE IN FOOD

It is interesting to discuss the formation of lysinoalanine (LAL) and acrylamide in food because they illustrate the formation of undesirable compounds from natural food components and present challenges to both food chemists and regulators. They also demonstrate the fascinating and elegant ways chemists discover how these compounds are formed in foods. LAL formation in proteins was discovered nearly 40 years before that of acrylamide. Before 1964, alkaline treatment of commercial proteins was routinely used to improve the flavor and texture, destroy toxins, and improve functionality (physical−chemical properties). In 1964, Patchornik and Sokolovsky (*34*) observed the formation of an unusual amino acid when they treated *S*-dinitrophenylated ribonuclease with alkali. They concluded that the new amino acid was the result of an addition reaction between the ε-amino group of lysine and dehydroalanine. They also reported the importance of cystine in the formation of dehydroalanine in proteins. This observation was important because it established dehydroalanine as the immediate precursor to LAL. Bohak (*35*) reported that LAL was formed in a variety of alkaline-treated proteins including lysozyme, papain, chymotrypsin, and phosvitin and in bovine serum albumin. Although lysine was not considered, products similar to LAL and lanthionine were observed by Eiger and Greenstein (*36*) in an earlier study of the addition of reaction products of sulfhydryls or amines with dehydroalanine. The importance of lysine in these addition reactions became apparent when a lysine cross-link was reported by Bohak. It soon became obvious (*37*) that very significant quantities of cyteine and lysine could be destroyed by alkaline treatment of proteins and, further, that production of LAL resulted in the loss of significant nutritional value and produced more toxic proteins. Following publication of these results of alkaline treatment of proteins, major commercial protein producers responsively decided to voluntarily curtail treatments of food proteins that produced over 100 ppm and later 50 ppm of LAL.

In April 2002 the Swedish National Food Administration announced at a press conference the finding of a wide range of amounts (up to 2300 ppb of acrylamide) in selected food samples. These levels were hundreds of times higher than those considered to be safe in drinking water. Just as in the discovery of LAL, acrylamide had not been previously reported in foods. Unlike LAL, acrylamide was a known neurotoxin and considered as probably carcinogenic to humans. The Swedish findings were released prior to publication in a scientific journal, so that food scientists throughout the world had no way of evaluating the research results. However, the World Health Organization (WHO) rapidly convened an expert consultation to undertake a preliminary review of new and existing data and research on acrylamide. The findings of that consultation called for further study of the levels and extent of acrylamide in food products, the mechanisms by which it is formed, bioavailability, exposure, and toxicological implications (*38*).

Scientists at the Procter & Gamble Co. and the Nestlé Research Center in Switzerland were among the first to elucidate the primary mechanism of formation of acrylamide in foods. Nestlé scientists found that heating asparagine and glucose at 185 °C yields significant amounts of acrylamide (*39*). Chemists at Procter & Gamble conducted some rather elegant work with radioisotopes to show how acrylamide was formed from asparagine and glucose (*40*).

FDA conducted its own analyses of acrylamide in foods. These analyses can be found on the FDA CFSAN Website (*41*). There are several other organizations with databases monitoring acrylamide in foods worldwide. These include the European Joint Research Centres Institute for Reference Materials and Measurements (*42*). It is not surprising that some of the highest levels of acrylamide were found in potato products. Potatoes contain high levels of asparagine. However, other food products such as cereal products were found to contain significant levels as well.

Scientists have found that the conditions of cooking and browning influence the level of acrylamide. Furthermore, consumers could significantly increase the levels of acrylamide through their cooking methods and degree of cooking (*43*).

Why has not FDA regulated the amount of acrylamide in foods? Several difficulties with this approach are readily apparent. Important studies regarding acrylamide are still ongoing. We are only a few months away from the NTP acrylamide rat/mouse bioassay being reported. FDA has recommended that food manufacturers examine their processes and reduce acrylamide whenever possible. There are several other possible reasons why there are not regulations limiting acrylamide. Perhaps the most important is that even after seven years of research, scientists do not yet know with any certainty whether the levels of acrylamide typically found in some foods pose a health risk for humans. Coupled with this is the question concerning at what level would a defect action level or tolerance level be set, considering the variety of foods that might contain acrylamide after cooking. It is also unlikely that change in high-temperature cooking methods such as frying, baking, toasting, and broiling will occur, especially as currently practiced by consumers. Because the precursors of acrylamide formation are common sugars and amino acids, it is impossible to eliminate them from our foods to avoid the formation of acrylamide. Cooking improves the flavor and texture of foods and reduces microbial pathogens, and regulating the temperature to which foods are cooked by consumers is difficult if not impossible. The best advice given by the U.S. National Cancer Institute is to follow established dietary guidelines. Eat a healthy, balanced diet that is low in fat and rich in high-fiber grains, fruits, and vegetables.

RECENT REGULATIONS

Regulations continue in response to consumer concerns about food safety. The project Bioshield Act of 2004 (*44*) authorized FDA to expedite its review of procedures to enable rapid distribution of treatments as countermeasures to chemical, biological, and nuclear agents that may be used in a terrorist attack against the United States.

Passage of the Food Allergy Labeling and Consumer Protection Act (*45*) in 2004 required the labeling of any food that contains a protein derived from any one of the following foods that as a group account for the vast majority of food allergies: peanuts, soybeans, cow's milk, eggs, fish, crustacean shellfish, tree nuts, and wheat. This Act, as with many of FDA's more modern regulations, has been accompanied by Guidance (*46*).

In 2007 it was reported that melamine was being found in pet food products being imported from China. Apparently, melamine was being added in place of the more expensive protein component in pet food products. Later it was found that melamine contamination occurred in infant formula products as well. These events led FDA to conduct a risk assessment on melamine and publish the results on its Website (*47*). This modern melamine addition to food shows that food adulterations continue today and may result in food safety concerns, just as they did in ancient times.

IMPACT OF FOOD CHEMISTRY RESEARCH IN THE FUTURE

It is clear that advances in chemistry and nutrition will continue to present many challenges to food regulators in the future. The past 20 years have seen the discovery of many bioactive and beneficial compounds in foods. We have also seen advances in genomics, proteomics, and nanotechnologies. As an example, some of the questions (*48*) posed by just one of these technologies, nanotechnology, are given in **Table 4** below.

Table 4. Regulatory-Related Questions Concerning Nanotechnology

synthetic or natural?
existing or new?
digestible?
food additive?
bioactive?
effect of food formulation/processing?

For a complete discussion of issues posed by food nanotechnology the reader is referred to the paper by Chau et al. (*49*). The answers to many of these questions can be provided only by additional research. And just as in the past, food chemists will continue to lead food regulation and provide understanding for food safety.

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