FOOD SAFETY, CHEMICAL CONTAMINANTS AND TOXINS

1. Introduction

A large number of chemicals, both natural and synthetic, may enter the food supply and pose potential food safety concerns. Some of these chemicals are intentionally added to food, eg, preservatives, colors, and flavors, while others eg, pesticides, metals, veterinary drugs, and food packaging materials, may inadvertently contaminate the food supply. Several potential food contaminants and toxins are identified in Table 1.

Note that the mere presence of a contaminant or toxin in food does not constitute a health threat. According to the sixteenth century Swiss Physician Paracelsus, who appropriately addressed the concept of dose and response, it is the amount of potentially unsafe chemical, not its presence or absence, that determines the potential for harm. There does exist a great variability in toxicological potency among chemicals entering the food chain; some may cause toxicological effects at very low doses while others require much higher doses before noticeable effects may be observed.

2. Regulation of Chemical Contaminants and Toxins in Food

Risk assessment and risk management practices have been widely developed as tools to aid in the regulation of food contaminants and toxins. Hazards from these chemicals may be introduced at all stages of the food chain (production, processing, distribution, retail, preparation, and consumption) and a variety of appropriate production and handling practices such as Good Manufacturing Practices and Hazard Analysis Critical Control Point (HACCP) programs have been established.

Risk managers at regulatory agencies are required to follow legislative mandates that may influence how the risk managers may interpret the results of risk assessments and consider other factors before making regulatory decisions. A variety of different risk-based models exist, including the following:

1. Zero risk, which presently applies to food additives that may induce cancer in humans or in animals. This risk model provides a zero tolerance for exposure.
2. Reasonable certainty of no harm (negligible risk), typically representing a risk of no more than one excess case of cancer per million persons exposed, or, for noncancerous effects, population exposure below levels of toxicological significance. In determining which exposure levels constitute a reasonable certainty of no harm, risk assessment models employ conservative (risk-magnifying) assumptions (1,2).
3. Risk balancing models that specifically require that both risks and benefits be considered before decisions are made (2).

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4. Technical feasibility, considering both the level of risk and the availability of current technologies to control the risk (2).

2.1. United States Regulation of Chemical Contaminants and Toxins.

The U.S. Food and Drug Administration (FDA) regulates food additives. A food additive must be demonstrated to be safe under its intended conditions of use before it can be approved. Many food additives, following review by qualified personnel, have been granted the status of Generally Recognized as Safe (GRAS). Others may be approved for use if they are not considered to be potentially carcinogenic and exposure estimates are below the Acceptable Daily Intake (ADI).

Potentially carcinogenic food additives, however, have a zero tolerance in food and are therefore not permitted regardless of the expected levels of exposure. They are regulated under the so-called Delaney Clause, a 1958 amendment of the Federal Food Drug and Cosmetic Act, which states that no substance that has been shown to induce cancer in humans or animals can be used as a food additive (3).

Other chemical contaminants and toxins regulated by the FDA incorporate different risk-based models for their regulation. Veterinary drugs, eg, are regulated by the negligible risk approach while negligible risk and risk balancing approaches are used in the regulation of potentially carcinogenic chemicals, eg, aflatoxins in peanuts and other foods and polychlorinated biphenyls (PCBs) in fish (4).

The U.S. Environmental Protection Agency (EPA), under provisions of the Safe Drinking Water Act, regulates drinking water contaminants. For noncarcinogenic drinking water contaminants, a negligible-risk approach is used where allowable levels are set to ensure that a fraction of the ADI is not exceeded. In the case of potentially carcinogenic drinking water contaminants, technological feasibility forms the basis for establishment of standards since it is recognized that zero risk is not technologically attainable. This approach results in the establishment of maximum containment levels at the lowest levels technologically feasible. In many cases, the cancer risks estimated at these levels are frequently below one excess cancer per 100,000 persons exposed although the cancer risks are higher in some cases.

The EPA also regulates pesticide residues in foods. Historically, the EPA has used a risk-balancing model that allows pesticides to be used when the potential benefits outweigh the potential risks. Examples of benefits could include the increased ability through pesticide use to produce an abundant, available, and affordable food supply by increasing crop yields and reducing production and consumer costs. Benefits could also include the reduction of plant stress with corresponding reductions in the production of plant or fungal toxins, and substitution impacts resulting from greater risks for environmental disruption or worker safety concerns from other less-effective pesticides following elimination of a more-effective pesticide.

In August 1996, the EPA shifted its risk-based model for pesticides in food from a risk-balancing model to a reasonable certainty of no harm. This change resulted from legislation that repealed the Delaney Clause with respect to pesticide residues following a National Research Council (NRC) report recommending such a practice (5), unsuccessful efforts by the EPA to adopt the NRC

recommendations (3), and a subsequent NRC report urging improvements in EPAs system of risk assessment, specifically with respect to the diets of infants and children (6). The new legislation instituted a "reasonable certainty of no harm" standard and required regulators to consider exposures and sensitivities of specific population subgroups, eg, infants and children, to consider the cumulative risks from families of pesticides that possessed common toxicological mechanisms of action, to consider the aggregate exposure to pesticides from dietary, water, and residential exposure, and to consider other types of toxicological effects, eg, endocrine disruption.

2.2. International Regulation.   The United Nations Food and Agriculture Organization (FAO) and the World Health Organization (WHO) established the Codex Alimentarius Commission in 1961–1962 to ensure consumer protection from exposure to a variety of food chemicals while also facilitating international trade. The Codex Alimentarius Commission develops standards, guidelines, and other recommendations that are developed by subsidiary bodies, eg, the Committee on Food Additives and Contaminants, the Committee on Pesticide Residues, and the Committee on Residues of Veterinary Drugs in Food. Risk management decisions under the auspices of the Codex Alimentarius Commission are based upon the consideration of risk assessment results, the weighing of policy alternatives, and selection and implementation of appropriate control options including regulatory measures.

3. Risk Assessment of Chemical Contaminants and Toxins in Food

The earliest "risk assessment" approaches for food safety involved trial-and-error methods to allow the distinction between safe and unsafe foods. Food testers used by ancient pharaohs or other royalty represented the first risk assessors while the pharaohs and kings and queens adopted the role of risk managers.

Today, the most accurate method to predict possible human risks from food is human epidemiology, which relies upon statistical analysis of data collected from human populations. Using epidemiological approaches, eg, it is estimated that one-third of human cancers may be traced to the diet (7) and it has been demonstrated that dietary changes can substantially decrease the rate of certain types of human cancers (8). Unfortunately, human epidemiology is severely limited by a number of factors, eg, the ethical considerations prohibiting human studies, the difficulty in measuring health effects that occur at low frequencies in a population, inaccuracy due to recall bias, difficulties identifying appropriate control groups not exposed to the chemical under study, and the inability to obtain human data on newly developed chemicals prior to their release. As a result, most risk assessments are based upon the results of animal toxicology studies and extrapolation of the results to predict possible human effects.

In 1983, the NRC released guidelines for performing chemical risk assessments, and identified four major components of risk assessment: hazard identification, dose-response assessment, exposure assessment, and risk characterization (9).

3.1. Hazard Identification.   Hazard identification is the process used to determine whether a particular chemical is causally linked to a specific health

effect. All of the available information concerning the chemical under consideration is evaluated from the results of epidemiological studies and experimental animal studies. Studies may have been conducted using short- (acute) or long-term (chronic) exposures and might include effects, eg, cancer, allergic reactions, birth defects, developmental defects, reproductive toxicity, neurotoxicity, immunotoxicity, or toxicity to the liver, kidney, lung, or skin.

The determination as to whether a chemical may or may not cause cancer is critical in contemporary risk assessment practices because different approaches are often used depending on whether the chemical causes cancer or not. Cancer studies are usually performed using chronic lifetime rodent bioassays and animals are frequently exposed to levels of chemicals representing the maximum tolerated dose (MTD) that does not alter the test animal's longevity because of noncancer effects. It has been argued that many chemicals may induce cancer at the MTD level from biochemical responses, eg, increased cell proliferation that might not occur at lower doses.

3.2. Dose-Response Assessment. Once a specific toxicological hazard (typically the most sensitive one in the most sensitive animal species) has been identified, the relationship between the dose of the chemical and the probability of occurrence of adverse effects can be estimated. To do this, risk assessors differentiate between threshold and nonthreshold effects.

Threshold effects are typically noncarcinogenic effects where it is assumed that toxic effects will not be observed until a minimum, or threshold, dose is reached. Toxicology studies are primarily developed to identify two dose levels: one above the threshold at which effects are seen [the lowest observed effect level (LOEL)] and one below the threshold [the no observed effect level (NOEL)]. Sometimes, these values are referred to as the lowest observed adverse effect level (LOAEL) and the no observed adverse effect level (NOAEL). Due to statistical, biological, and practical limitations in the number of doses studied in toxicology studies, it is difficult to accurately assess the degree to which the NOEL or LOEL estimates approximate the toxicological threshold dose. As a prudent measure, the NOEL is usually selected as a conservative estimate of the threshold.

Since NOEL values are usually derived from animal toxicology studies and not from human toxicology studies, risk assessors make use of uncertainty factors that allow extrapolation from the results of small homogenous groups of animals to predict toxicological thresholds for large and heterogeneous human populations. The most common uncertainty factor is 100 and is rationalized as including a 10-fold uncertainty factor (assuming that humans, in general, are 10 times more sensitive to the toxicological effects than the animals studied), multiplied by an additional 10-fold uncertainty factor for human variation that assumes that some members of the human population are 10 times more sensitive than the average human. In some cases, additional 10-fold uncertainty factors are incorporated to provide greater protection for infants and children or for women of childbearing age.

An ADI is calculated by dividing the NOEL by the selected uncertainty factor. The ADI represents the estimate of the amount of exposure to a food chemical that can be consumed on a daily basis by humans without anticipated

harm (reasonable certainty of no harm). An analogous term, the reference dose (RfD) is used by the EPA.

The assessment of cancer risks differs from the risks of noncancer effects due to differential treatment of toxicological thresholds. For carcinogenic hazards, it is frequently assumed that a threshold does not exist and that any level of exposure may present a quantifiable cancer risk (although the probability is still related to the dose); this implies that a NOEL may not exist for carcinogenic effects.

While it is possible that some carcinogens may indeed act without a toxicological threshold, many others, eg, those that induce thyroid tumors or those that induce tumors due to increased cell proliferation, may act using toxicological mechanisms that are consistent with thresholds. Currently, though, most carcinogenicity risk assessment models still use nonthreshold assumptions.

To quantitatively estimate human cancer risks from exposure to chemicals in food, the results from high dose animal cancer studies are extrapolated to predict human risks at low exposures. Several mathematical models have been developed to do so and each model results in a value known as the cancer potency factor, or Q^*. The Q^* values vary dramatically among different models because of the different assumptions used in each model. The most commonly used model is the linearized multistage model that assumes that a cell goes through a specific number of different stages and that the probability of a "hit" on the cell by the carcinogenic chemical, ultimately resulting in the development of cancer, is stage specific. At the lowest exposure levels, it is assumed that the relationship of the dose of the carcinogen and the excess risk of cancer is linear.

3.3. Exposure Assessment. Prior to the determination of risks from exposure to chemical contaminants and toxins in food, the information obtained from the hazard identification and dose-response assessment processes need to be combined with an estimate of the amount of exposure, or dose, likely to occur. This requires information concerning both the amount of chemical contaminants or toxins on foods, as well as information concerning consumption patterns of foods containing these chemicals. Both chemical levels and food consumption estimates may be variable and their estimation may necessitate the need to make several assumptions.

The nature of the food chemical under study can dramatically influence the ease and accuracy of the exposure assessment. For some chemicals, eg, food additives, the concentration may be well known and relatively constant. For other incidental chemicals in food, eg, pesticide residues, hormones, antibiotics, metals, and other environmental contaminants, concentration levels may vary dramatically among samples. This variability may be heightened in cases where reliable and representative monitoring data are limited.

Another challenge is the acquisition of useful and accurate food consumption data. Most data of this type are collected from national food consumption surveys. Survey types include food disappearance data, household disappearance data, dietary histories, dietary frequencies, 24-h recalls, food records, weighted intakes, and duplicate portions (10). The most common food consumption estimates used for dietary risk assessment purposes are those derived from the results of the U.S. Department of Agriculture (USDA) nationwide food

consumption surveys based upon 3-day dietary records describing the types and amounts of foods consumed at home and away from home.

Historically, approaches to estimate food chemical exposure have relied upon deterministic models that develop "point estimates" derived from assuming a particular concentration level of the chemical being studied and a specific food consumption estimate. The choice of concentration and food consumption levels can dramatically influence the ultimate estimates of exposure and care should be taken to justify the choices of concentrations and food consumption estimates. As an example, an NRC report on pesticide exposure and possible cancer risks calculated exposure estimates assuming that all pesticide residues were present on all commodities for which the pesticides were registered for use and that all residues were present at the maximum allowable levels (5). A subsequent study, using more realistic estimates of pesticide residue levels, showed that the NRC exposure estimates were hundreds to tens of thousands of times exaggerated and in many cases suggested greater than negligible cancer risks although the more accurate data showed cancer risks in the negligible range (11).

Deterministic methods for exposure assessment are frequently being replaced by probabilistic methods that take advantage of improved computational capabilities. Realistically, both chemical concentration levels and food consumption patterns exist as distributions rather than as specific points. Through the use of statistical convolution, it is possible to combine the concentration distributions with the food consumption distributions to develop an exposure distribution. Not only is this approach capable of determine the average (50th percentile) exposures, but it also can determine exposure levels at the upper ranges (95th, 99th, 99.9th percentiles) that may be of interest in determining the risks from exposure to chemicals possessing acute hazards.

3.4. Risk Characterization.   The final stage of the risk assessment process involves a description of the nature and magnitude of risk by comparing estimated human exposure levels with levels of toxicological significance.

In the case of noncarcinogenic effects, the risk characterization process typically compares the exposure estimates to the ADI or RfD. In cases where the exposure level is below the ADI or RfD, the risk is considered to be negligible and represents a reasonable certainty of no harm. Note that in cases where the ADI or RfD is exceeded, it should not be implied that harm will ensue since the ADI or RfD does not represent a human toxicity threshold, but rather a level several times lower than anticipated threshold levels observed from animal toxicology studies.

For carcinogenic effects, estimated cancer risks are obtained by multiplying the estimated levels of exposures with the cancer potency factors. Frequently, such results are reported to indicate an estimate of a particular number of cancers estimated per million people exposed to the chemical. To properly interpret such findings, it is critical to understand that the actual numbers presented typically represent the upper bounds of cancer risks calculated using conservative treatment of several uncertainties, eg, nonthreshold dose–response behavior, and, as such, do not accurately reflect true cancer rates (12). Cancer risks below one excess case of cancer per million persons exposed have arbitrarily been considered to represent negligible cancer risks (5).

4. Examples of Chemical Contaminants and Toxins in Food

As Table 1 shows, there are several types of chemical contaminants and toxins that may enter the food supply. This article highlights four areas of contemporary concern: pesticide residues, dioxins, acrylamide, and chemical components in organic foods.

4.1. Pesticide Residues.   Pesticides refer to a broad class of chemical agents that control pests, eg, insects, weeds, fungi, nematodes, mites, bacteria, rodents, snails, and algae. In the United States, there are >20,000 pesticide products registered for use; some common examples are listed in Table 2. According to recent market estimates, world pesticide use exceeded 5.0 billion lb in 2000 and 2001 while U.S. pesticide use exceeded 1.2 billion lb in each of those years (13). The agricultural use of pesticides in the United States was 772 million lb in 2000 and 675 million lb in 2001, with herbicides/plant growth regulators representing 64% of agricultural pesticide use in 2001, followed by nematicides–fumigants (15%), insecticides/miticides (11%), and fungicides (6%) (13).

The agricultural use of pesticides does not necessarily result in residues on foods. Many pesticides are applied to nonfood crops (ie, cotton, ornamental plants, weeds) while others may be applied prior to the formation of the edible portion of the plant or early enough before harvest to allow residues to dissipate below detectable levels. Nevertheless, agricultural application of pesticides does frequently result in food residues and has been the subject of consumer concern. Consumer attitude surveys indicate that 72–82% of the U.S. population considers pesticide residues to be a major concern (14). This perceived concern is not consistent with food safety rankings of the FDA, where pesticides are ranked as the (FDAs) fifth food safety priority and of less concern than (1) microbiological contamination, (2) nutritional imbalance, (3) environmental contaminants, and (4) naturally occurring toxins (15). Additional risks from pesticides besides those from dietary exposure include occupational exposure, environmental contamination, reduction of natural pest enemies, effects on fish and wildlife population, livestock toxicity, honeybee losses, evolved pesticide resistance, and creation of secondary pest problems.

Pesticides in the United States are regulated on a risk-balancing basis and the use of pesticides is only permitted when the benefits of the use of the pesticide are considered to outweigh any risks. In the case of pesticides that may leave residues on foods, the US EPA sets allowable levels, known as tolerances, that are specific for the pesticide and crop on which it may be found. Before approving a pesticide tolerance, the EPA must certify that the pesticide poses a reasonable certainty of no harm according to the Food Quality Protection Act (FQPA) of 1996. In making this certification, the EPA must consider the potential increased exposure and susceptibility of infants and children, the aggregate exposure to the pesticide from food, water, and residential use, and the cumulative exposure to members of pesticide families that share a common toxicological mechanism of action.

If the pesticide does not meet the "reasonable certainty of no harm" criteria (typically demonstrating a cancer risk of more than 1 excess case of cancer per 1

million persons exposed or a noncancer exposure of a defined population subgroup to an amount that exceeds the RfD), tolerances for the pesticide will not be established. If the "reasonable certainty of no harm" criteria is met, the EPA will allow pesticide tolerances to be established at levels high enough to ensure that pesticide uses complying with established use practices will not result in residues in excess of tolerances. As such, tolerances should be considered as enforcement tools to indicate compliance with regulations, but not as barometers of human safety (16). Violative residues occur when residues of a particular pesticide on a specific commodity are detected in excess of the established tolerance, or, more frequently, when residues of a pesticide are detected on a commodity for which a tolerance has not been established.

While the EPA registers pesticides, determines appropriate use practices, and establishes tolerances, the FDA is primarily responsible for the monitoring of food produced or imported into the United States for pesticide residues. Sampling programs for FDAs pesticide residue monitoring are not random or representative of the food supply as a whole, but are skewed to maximize the chances of identifying violative residues.

In 2003, the FDAs Regulatory Monitoring Program analyzed 2344 domestic and 4890 imported food samples for pesticide residues; results are shown in Fig. 1. Pesticide residues were detected in 37.3% of domestic samples and in 28.2% of imported samples. Violations were higher (6.1%) in imported samples than in domestic samples (2.4%). Only 0.4% of domestic samples and 0.5% of imported samples contained residues that exceeded tolerances; the vast majority of violations for both domestic and imported samples involved the detection of pesticides on commodities for which tolerances were not established (17).

Since tolerances should not be considered to be safety standards, comparisons of residue findings with tolerance levels demonstrate that pesticides are typically applied in accordance with the legal directions, but are not particularly useful for risk assessment purposes. The FDA also conducts another study, the Total Diet Study, in which market baskets containing 285 different food items are analyzed annually for pesticide residues and other contaminants after they are prepared for consumption. Results from this study, when combined with crude estimates of consumption of the types of foods analyzed, allow calculation of potential daily dietary exposure to pesticides. The FDA last published its pesticide exposure estimates in 1992, at which time the vast majority of pesticides showed daily dietary exposure at levels far <1% of the ADI (18). Placed in perspective, a daily dietary exposure at 1% of the ADI represents an exposure 10,000 times lower than the level that does not produce noticeable effects in laboratory animals, assuming a 100-fold uncertainty factor is used. Such a finding explains why FDA considers the potential dietary risks from pesticide residues to be much lower than the risks from microbiological contamination or other food safety issues.

4.2. Dioxins. Dioxins represent a family of organic chemicals that exist widely as environmental contaminants. Of greatest toxicological concern are the polychlorinated dibenzo-*p*-dioxins (PCDDs), which are structurally and toxicologically related to the polychlorinated dibenzofurans (PCDFs) and to the polychlorinated biphenyls (PCBs). Since these families of compounds possess common toxicological and structural features, they will be considered to

represent "dioxins" for the purposes of this article. There are >200 dioxin-related congeners differing in the locations and extent of halogenation; each congener possesses unique toxicological and chemical properties.

Dioxins are primarily introduced into the environment as a result of combustion processes. Both PCDDs and PCDFs have been identified from cigarette smoke, industrial and municipal waste incinerators, automobiles, and from coal, oil, or wood burning power plants. They are also produced naturally through combustion processes resulting from forest fires and volcanic eruptions.

The PCDDs and PCDFs have also been produced as impurities of organic synthesis. The most toxic dioxin congener, 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) is produced in the synthesis of the herbicide 2,4,5-T, a notorious component of Agent Orange used during the Vietnam War. The herbicide 2,4,5-T has been banned due to TCDD contamination concerns, but health concerns regarding the exposure of military personnel to TCDD and other dioxin impurities are still frequently voiced today.

The PCBs have been synthesized for use as capacitors in electrical machinery and as dielectric fluids in transformers as a result of their inflammability. They are frequently detected in the environment and pose toxicological concerns today even though the synthesis and industrial use of PCBs was significantly reduced in the 1970s.

While data concerning the contamination of the food supply from dioxins is still not comprehensive, dioxins are known to be highly fat-soluble and are known to accumulate in the fat of birds, fish, food animals, and in humans. It has been estimated that >95% of human exposure to dioxins may result from the dietary intake of animal fats, with the major food sources identified as fish, poultry, meats, milk, and milk products (19). Dioxins are excreted into human breast milk and may be ingested by nursing infants.

At high levels of exposure resulting from chemical accidents or occupational exposures, dioxins have caused a number of human health effects including chloracne, skin rashes, skin discoloration, and liver damage. Most recently, Ukrainian politician Viktor Yuschenko was diagnosed to have been poisoned by dioxin, presumably resulting from political motivations.

Chronic dioxin concerns include cancer, reproductive effects, and developmental effects. 2,3,7,8-tetrachlorodibenzo-p-dioxin has been classified by the International Agency for Research on Cancer as a human carcinogen.

In addition to difficulties determining dioxin levels in foods, risk assessment is also complicated by the presence of large numbers of dioxin congeners, each possessing its unique toxicological and chemical characteristics. A Toxic Equivalency Factor (TEF) approach is often used that assigns potency factors to each congener relative to that of TCDD. To calculate total dioxin exposure, the dietary contributions for each of the dioxin congengers are determined by multiplying the exposure levels with the TEF; the contributions of all congeners are then combined to express exposure on the basis of TCDD equivalence.

The WHO established a Tolerable Daily Intake (TDI) for TCDD equivalence at 10 picograms per kilogram body weight per day (pg/kg/day) in 1990; the TDI has subsequently been reduced to the range of one to four pg/kg/day (20). Estimates of consumer exposure in various countries to dioxin are close to the TDI, including estimates from the United Kingdom (1.8 pg/kg/day), Italy

(0.7 pg/kg/day), Norway (1.4 pg/kg/day), Spain (2.4−3.5 pg/kg/day), and New Zealand (0.2 pg/kg/day) (20). While the FDA Total Diet Study has included dioxin analysis since 1999, the FDA has not released its own exposure estimates. Nevertheless, the EPA has recommended that consumers follow established dietary guidelines to limit their exposures to dioxins.

4.3. Acrylamide.   Acrylamide has a number of industrial uses including as a soil conditioner, as a coagulant in water treatment and purification, and as a construction aid for the building of tunnels and dams. Toxicologically, it has raised concerns due to its listing by the International Agency for Research on Cancer as "probably carcinogenic to humans" as a result of several animal cancer studies. The concerns, until recently, focused primarily upon occupational exposure to acrylamide among industrial, manufacturing, and laboratory workers.

Swedish researchers identified hemoglobin adducts of acrylamide in blood samples from humans. It was expected that such hemoglobin adducts would be found in the blood samples of smokers since acrylamide is a known component of tobacco smoke, but results also indicated that acrylamide hemoglobin adducts were found in blood samples of nonsmokers, suggesting other sources of acrylamide exposure, eg, the diet. In April 2002, Swedish researchers published research demonstrating the presence of acrylamide in a variety of foods with the highest levels found in fried and baked foods (21).

Subsequent studies were performed throughout the world to determine the mechanisms for acrylamide formation in foods. A variety of mechanisms have been proposed, and it appears that the most prominent mechanism involves reaction of the amino group of the amino acid asparagine with the carbonyl group of a reducing sugar at the elevated temperatures used during baking and frying (22). Since potatoes are high in asparagine and in reducing sugars, and are frequently prepared using frying or baking, acrylamide levels in processed foods containing potatoes are frequently high relative to acrylamide levels in other foods. Initial Swedish findings demonstrated levels of 150−4000 parts per billion (ppb) of acrylamide in potato products while lower levels (5−50 ppb) were found in protein-rich foods that were heated. Unheated or boiled foods did not demonstrate acrylamide at levels above the detection limit (5 ppb). Similar findings have been reported by the FDA, with the highest levels observed in french fries (29 samples, range 117−1030 ppb) and in potato chips (40 samples, range 117−2762 ppb) (23). Monitoring studies also indicate significant variability among different lots of the same commercial food products.

Acrylamide toxicology studies demonstrate that it may cause cancer and has been associated with reproductive toxicity, genotoxicity, and neurotoxicity. Epidemiological studies of workers exposed to acrylamide have not demonstrated an increase in cancer, but have observed neurotoxic effects related to large acute exposures to acrylamide, resulting in nervous system damage, weakness, and incoordination of limbs.

While humans have been consuming acrylamide in their diets for a long time, heightened concern has arisen due to its recent discovery in foodstuffs. At the present time, risk assessments are in progress and the FDA, which recommends that consumers continue to eat a balanced diet and minimize consumption of trans and saturated fats, has not established regulatory limits for acrylamide. The state of California, on the other hand, has filed lawsuits against

nine food companies to force them to label french fries and potato chips sold in California with a consumer warning indicating the products contain a chemical known by the state of California to cause cancer.

4.4. Chemical Components of Organic Foods.   The popularity and sales of organic foods has risen dramatically in the past several years; it has been estimated that organic sales growth has been at the rate of ~20% per year since 1990 and consumer sales in the United States reached $13.8 billion in 2005 (24). Surveys have frequently indicated that many consumers purchase organic foods because of the perceived health and nutrition benefits of these foods compared with conventional foods.

Growth in the organic foods industry has also resulted from the adoption of national uniform organic standards in the United States that were first announced in 2000 and fully implemented in 2002. The standards prohibit, under most circumstances, the use of synthetic pesticides and fertilizers, recombinant DNA technologies, and irradiation in the production of organic foods. Many other standards have been developed to address the use of organically approved ingredients, certification requirements, the use of organic labels, animal handling conditions, and transitions of fields from conventional to organic status.

Pesticide residue monitoring programs performed by the U.S. Department of Agriculture, the California Department of Pesticide Regulation, the Consumers Union, and in Europe have enabled comparisons of pesticide residue levels between organic and conventional produce. While the occurrence of residues in organic foods was much lower than the occurrence in conventional foods, pesticide residues were frequently detected in organic produce. In the largest study, conducted by the U.S. Department of Agriculture, 73% of conventional foods showed detectable residues of pesticides while 23% of the organic foods showed detectable residues. Slightly less than one-half of the residues detected in the organic food samples represented environmentally persistent banned chlorinated hydrocarbon pesticides that may have resulted from uptake from contaminated soil although 13% of the organic food samples showed the presence of pesticides that were presently allowed for use on conventional crops. The ratios of detected residues on conventional crops relative to those on organic crops were 3.2 for the U.S. Department of Agriculture monitoring program, 4.8 for the California Department of Pesticide Regulation monitoring program, 2.9 for the Consumers Union study, and 4.1 for residue monitoring in Belgium (25).

A number of studies have conclusively demonstrated that nitrate levels in organic foods are usually lower than those in conventional foods. Data from foods sold in Belgium demonstrated a mean nitrate level of 1703 parts per million (ppm) for organic foods and 2637 ppm for conventional foods (26). These results presumably arise from the greater contribution of nitrates in synthetic fertilizers frequently used in conventional food production.

Studies demonstrating an increase in nutrients in organic foods relative to conventional foods have frequently been inconclusive; there are several examples where nutrient levels were elevated in organics and others where nutrient levels were elevated in conventional foods (25). Most recently, a number of controlled studies have compared organic and conventional production with respect to many presumed antioxidant chemicals, eg, polyphenolic compounds. Greater

levels of polyphenolics have frequently resulted from organic production methods as compared with conventional production methods. Two major hypotheses have been advanced to explain these differences. One considers the impacts of different fertilization practices on plant biochemistry and metabolism and concludes that the synthetic fertilizers used in conventional production may accelerate plant growth and development at the expense of the synthesis of plant secondary metabolites (chemicals not essential to the life of the plant), eg, organic acids, polyphenolics, and chlorophyll.

The second hypothesis concerns the response of plants to stress factors eg, insect, weed, and plant pathogen attacks. Organic production methods, which are frequently limited in the use of insecticides, herbicides, or fungicides to control plant pests, may put greater pest pressures on the plants, thus requiring the plants to use their resources in the synthesis of their own chemical defense mechanisms. The increases in plant polyphenolics in some organic foods have been attributed to their increased production resulting from plant defense. In the case of plant polyphenolics, this increase is of potential health benefit due to the presumed antioxidant effects attributed to the plant polyphenolics. In other cases, however, the elevation of plant secondary products resulting from plant stress could lead to the development of increased levels of naturally occurring toxins, eg, glycoalkaloids, cyanogenic glycosides, furanocoumarins, or mycotoxins (25).

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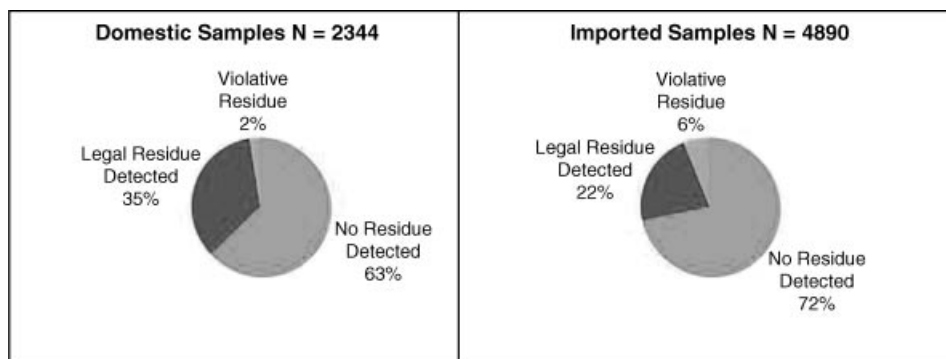
Fig. 1.   Results from FDAs 2003 Pesticide Residue Regulatory Monitoring Program (17).

Table 1. **Potential Food Contaminants and Toxins**[a]

Food Additives

   preservatives
   colors
   flavors
   stabilizers
   supplements

Biogenic Compounds

   plant toxins or phytotoxins
   bacterial toxins,
   enterotoxins
   mycotoxins
   marine toxins (eg, algal toxins responsible for paralytic shellfish poisoning and
      diarrhoetic shellfish poisoning)

Residues

   processing aids (catalysts, filtration aids, antifoaming agents, extraction solvents, etc)
   pesticides
   animal feed additives
   veterinary or therapeutic drugs (medicines, antibiotics, hormones)
   environmental ccontaminants (heavy metals, industrial chemicals, eg, polychlorinated
   biphenyls and polycyclic aromatic hydrocarbons)

Contaminants

   processing contaminants (eg, mutagenic heterocyclic amines)
   food packaging migrants (plastics, waxes, inks, etc,). Also called indirect food additive

Others

   (adulterants, chemicals used for tampering)

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Table 2. **Some Pesticide Classes and Examples of Each Class**[a]

Pesticide	Examples
Insecticides	
chlorinated hydrocarbons	dicofol, methoxychlor
	DDT[b], aidrin[b], dieldrin[b] chlordane[b]
organophosphates	parathion, malathion, phosdrin, diazino
	chlorpyrifos, azinphos-methyl
carbamates	aldicarb, carbaryl, carbofuran
pyrethroids	permethrin, cypermethrin
Herbicides	
triazine	atrazine, cyanazine
phenoxy	2,4 D
quaternary ammonium	paraquat
benzoic acids	dicamba
acetanilides	alachlor, metolachlor
ureas	linuron
Fungicides	
inorganic	sulfiir
ethylenebisdithiocarbamates	maneb, mancozeb
chlorinated phenols	pentachlorophenol

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[b]Banned in the United States.