Trends in Food Safety

Ronald Walker

Food Safety Group, School of Biological Sciences, University of Surrey, Guildford, England, United Kingdom

In order to determine a trend, i.e., a slope on the curve of change in a variable with time, it is necessary to look at more than one point. By looking at the historical changes it is possible to see how the variable has altered in the past and obtain a better perspective of potential future changes—although with the increasing rate of scientific and technological change, prediction is becoming increasingly difficult and uncertain. It is proposed, therefore, to look at the historical development of food safety issues and at the evolution of regulatory mechanisms aimed at food safety assurance. Against this backdrop, and in the light of new developments in agriculture and food technology, emerging and future issues may be identified. The requirements for new mechanisms of safety assurance and consequent research needs can then be established.

HISTORICAL DEVELOPMENTS IN FOOD SAFETY

Although legislation aimed at ensuring the safety of food is not new, and the Law of the Hittites bears some similarity to the general provisions of 20th-century food law in the United Kingdom (Table 1), laws on food adulteration in Europe and America up to the beginning of this century were primarily drafted for excise rather than health purposes. The first Food and Drug Act, containing significant sections related to food safety and consumer protection, was promulgated in the United Kingdom in 1875 and in the USA in 1906. Under the provisions of these general acts and later revised versions, specific regulations relating to food safety (hygiene regulations, regulations on various classes of food additives, contaminants, and packaging materials) have been issued subsequently.

The approaches that may be adopted to regulating additives or other chemicals in food may follow two principles:

(a) Principle of interdiction: positive lists of permitted additives, all others prohibited;
(b) Principle of abuse: negative lists of prohibited substances, anything else permitted (on the vendor's responsibility for safety under the general food law).
As early as 1923 in the United Kingdom, a Ministry of Health Committee on the use of colors and preservatives in food advised the adoption of the principle of interdiction in recommending the establishment of a list of colors considered non-injurious to health; the government of the day ignored the advice and merely produced a negative list prohibiting the use of five synthetic colors and one natural color (gamboge) known to be harmful (1). It was not until the 1950s that the principle of interdiction was introduced into United Kingdom food law with the establishment of the first permitted list of food colors in 1957 (2).

The reluctance of governments to go down this track of permitted lists was almost certainly influenced by the implicit endorsement of the safety-in-use of listed food additives and hence the need to have a suitable infrastructure for safety evaluation and assurance. At the beginning of the 1950s there was no clearly identifiable science of food toxicology, only an ad hoc and often inappropriate application of the same principles that had been applied to forensic and drug toxicology with too great an emphasis on acute toxicity and a poorly thought out strategy for evaluation of the chronic effects of exposure to low doses of food additives or contaminants over a life span. So even the ground rules for the toxicological evaluation of additives and contaminants needed to be defined; a means was also needed for translating the toxicological data to safe levels of human exposure, together with a machinery for regulation and enforcement to ensure that these levels were not exceeded.

The rapid developments in food technology during the 1940s and 1950s, initially catalyzed by the Second World War, led to an increased need to control potential hazards from deliberate food additives and residues of processing aids, solvents, and packaging materials. In the same period, the primitive agrochemical pesticides (e.g., sulfur, arsenicals, Bordeaux mixture) were being replaced by the modern pesticides (organochlorines, organophosphates, carbamates etc.) raising problems of residues in food, possible accumulation in the food chain (organochlorines), or acute toxicity to farm workers, and the related environmental and ecological concerns. In 1953, the Sixth World Health Assembly indicated that the increasing use of chemical substances by the food industry created a new public health concern that might usefully be investigated (3). Following a recommendation by the WHO Executive Committee in 1954 (4), the first Joint FAO/WHO Conference on Food Additives met in 1955 and in turn recommended the directors-general of FAO and WHO to convene one or more expert committees concerned with the technical and administrative aspects of food additives (5), viz:
(a) to formulate general principles governing the use of food additives, with special reference to their legal authorization, on the basis of considerations such as innocuity, purity, limits of tolerance, and the social, economic, psychological, and technological reasons for their use . . . , and

(b) to recommend, as far as is practicable, suitable uniform methods for the physical, chemical, biochemical, pharmacological, toxicological, and biological testing of food additives and of any breakdown products formed during food processing . . . and for the assessment and interpretation of the results.

These recommendations led to the establishment of the Joint FAO/WHO Expert Committee on Food Additives (JECFA) in 1956.

Slightly later, following a joint meeting of the WHO Expert Group on Pesticide Residues and the FAO Panel of Experts in 1961, the Joint FAO/WHO Meeting on Pesticide Residues (JMPR) was set up and has met regularly since.

The work of the JECFA led to the establishment of principles for the toxicological testing and safety evaluation of food additives and contaminants, and to the emergence of the concepts of the Acceptable Daily Intake (ADI, tolerable daily or weekly intake for some contaminants), concepts which have been widely adopted by national and supranational regulatory authorities, such as the EC Scientific Committee for Food. Based on experience over 35 years in the toxicological assessment and safety evaluation of a wide range of food additives, solvents, processing aids, heavy metals, and other contaminants—and more recently enzymes used in biotechnological processes of food manufacture—the basic principles regularly have been refined and updated, leading to the publication of a consolidated, updated collation of these principles in the International Program on Chemical Safety, Environmental Health Criteria Series in 1987 (6). The parallel work of the JMPR led to the additional concept of Maximum Residue Limits (MRL) for pesticides in foods as a means of ensuring not only that the ADI would not be exceeded but also that the residue levels should be as low as possible, consistent with efficacy and good agricultural practice. The principles adopted by the JMPR for the toxicological assessment of pesticides recently have also been published in consolidated form (7).

The activities of the JECFA and JMPR reflect the emergence of the science of food toxicology as a mature discipline and the evolution of a safety evaluation mechanism which is able to respond to scientific advances in toxicology and technological change in agriculture and the food-processing industry. However, some novel technological processes have posed special problems that have required different approaches; one such example is food irradiation. The question of appropriate studies required to ascertain the wholesomeness of irradiated food was initially discussed by an expert committee sponsored by the FAO, WHO, and the International Atomic Energy Authority (IAEA) in 1964 (8), and subsequent joint meetings have addressed the issues of particular raw materials/products and radiation doses (9–11). These committees have considered microbiological, nutritional, and toxicological aspects of the process and have made recommendations on acceptable radiation doses to be applied to particular commodities; future research needs have also been identified.
The acceptance of food irradiation as a process has been long delayed in many countries and still encounters considerable resistance among consumers. Although it can no longer be considered a truly novel process, the issues surrounding food irradiation continue to be debated and the topic will therefore be discussed further below in relation to future trends and research needs.

The emphasis in this historical review has so far been on the safety of chemicals deliberately or adventitiously added to food during production or processing. Indeed, in the public perception these have dominated the food safety scene until very recently, with relatively little attention being paid to microbiological hazards (including mycotoxins) and natural toxicants. Although legislation on food hygiene has been promulgated, and continually refined in all developed countries, the problem of microbiological food poisoning has been relatively persistent, with a seemingly intractable hard core of cases occurring every year. Indeed, the statistics on food poisoning in the United Kingdom have shown an upward trend in recent years (Figs. 1 and 2) despite the development of Hazard Analysis Critical Control Point (HACCP) systems in the food processing sector. New production and processing procedures, products, and retailing practices have contributed to the changing patterns of food poisoning and the emergence of new food pathogens, which in turn have created new research needs and regulatory action. However, only recently has a heightened public awareness emerged, largely in connection with salmonella in poultry, including S. enteritidis in eggs, and Listeria monocytogenes in some cheeses and refrigerated foods. This has added a greater degree of urgency to regulatory control procedures. The impact of novel foods and retailing methods on microbiological hazards and research needs are discussed below.

Natural toxicants in traditional or new food sources have never featured highly either in the public perception of food hazards or in regulatory activity. However,
FIG. 2. Incidence of infections by Salmonella and *Campylobacter jejuni*; data from Communicable Disease Report 88/52, Public Health Laboratory Service.

historically, these toxicants are known to have contributed to human mortality and morbidity, and a number of natural flavors (e.g., saffrole) and colors (e.g., gamboge) have been withdrawn or prohibited on toxicological grounds. Recent trends to replace food additives with natural alternatives ("free from artificial colors and flavors") are thus reflections of a perceived rather than a real risk reduction in many cases.

Another area that historically has received little attention is that of potential toxicants/carcinogens produced in conventional preparation and cooking procedures in domestic or catering situations. While the formation of polycyclic aromatic hydrocarbons in grilled or roasted foods has been recognized for many years, and more recent research has revealed the formation of some very potent heterocyclic mutagens in meat and fish (over)cooked in this way (13), little has been done to interpret and communicate effectively this information to the lay public.

Perceptions of risk therefore remain distorted. The Marabou Symposium on Food and Cancer in 1978 (14) concluded that, "of the potential sources of harm in foods, the largest by far are, first, microbiological contamination and, next, nutritional imbalance. Risks from environmental contamination are about 1,000 times less and risks from pesticide residues and food additives can be estimated as about a further 100 times smaller again. Naturally occurring compounds in food are far more likely to cause toxicity than intentional food additives."

However, the public perception (at least until recent alarms over microbial food
poisoning) has been almost the converse of this, leading to very active lobbies against additives, pesticides, food irradiation, and novel foods and processes.

FUTURE DEVELOPMENTS AND RESEARCH NEEDS IN FOOD SAFETY

Against the above background, it is evident that there is still a need to improve the existing methods of safety evaluation and assurance and to develop these methods to keep abreast of scientific and technological developments. The broadening use of biotechnology and genetic engineering in food production and processing, the development of totally novel foods or ingredients (including nutrient replacers or "displacers"), and the changes in food retailing techniques are raising new food safety issues and questions requiring scientific research to provide the answers.

The emergence of the animal rights movement has spearheaded a growing popular revulsion against animal experimentation seen as unnecessary or for trivial reasons. In this context, food additives—and to some extent pesticides—are commonly viewed as trivial and unnecessary—a view strengthened to some extent by food marketing strategies emphasizing freedom from additives, or "organically grown." This will clearly add pressure to develop alternative methods of safety evaluation using in vitro techniques. The ecological ("green") consequences of the activities of the agricultural and food-processing industries will also need to be taken into account. Food safety questions are increasingly acquiring a social, ethical, and political dimension that will have to be recognized, and the solutions to these questions will not always be scientifically driven.

With this in mind, crystal gazing into future trends and research to ensure safer foods into the 21st century reveals a number of emerging issues for attention.

Microbiological Issues

Animal Production and Products

As indicated above, there has been a rising trend in the incidence of salmonellosis associated with poultry and eggs in recent years. The extent to which this is due to intensive production methods and the recycling of offal in feed is not clear but, more generally, methods for decontamination of animal feed by economically viable processes (e.g., organic acid treatment of poultry feed) will probably be needed. In this context, studies on the effects of irradiation of feed not only on the concentration of strains of Salmonella but also on emerging pathogens such as Listeria monocytogenes, Campylobacter jejuni, and Yersinia enterocolitica may suggest possible solutions.

The emergence of bovine spongiform encephalopathy in cattle superimposed on the long-standing occurrence of scrapie in sheep has also called into question the safety of practices of recycling slaughterhouse waste and other offal in animal feed, a practice which has now been discontinued in some countries pending more detailed
investigations of the effects of feed processing conditions on the putative infective agent.

Meanwhile, the nonscientific considerations mentioned above may themselves bring about a reappraisal of intensive production methods.

Changes in Food Manufacture, Packaging, and Retailing

The effects of changes in food manufacturing processes, packaging, and retailing will continue to need constant monitoring, particularly in regard to the emergent pathogens. The microaerophilic *Campylobacter jejuni*, and *Listeria monocytogenes* which can grow at chill temperatures, have increasingly been implicated in human pathogenesis and raise questions concerning packaging in low oxygen tension conditions and the production, retailing, storage, and shelf life of cook/chill foods respectively. In fact, although the incidence of listeriosis remains low relative to Campylobacter or Salmonella infections, the rise in incidence (Fig. 3) has brought about a major reappraisal of methods of production and retailing of cook-chill foods in the United Kingdom. There is a particular need with these emergent pathogens to have a greater appreciation of the effects of environmental factors on survival and growth through the processing and distribution chain.

There is also a continuing need to improve techniques for monitoring food hygiene throughout the chain, in particular to develop rapid and specific methods for assessment of microbial status in hazard analysis (HACCP) schemes for total quality assurance. In the absence of these measures, it is difficult to see how the upward trend of food poisoning outbreaks and the emergence of new sources of infection and intoxication are to be stemmed.

![Graph of Listeriosis in England and Wales](image)

**FIG. 3.** Listeriosis in England and Wales: laboratory reports to the UK Public Health Laboratory Service Communicable Disease Surveillance Centre.
Finally, the reaction against the use of fungicides in agriculture and storage, and of preservatives in processed foods, may lead to an increased hazard from mycotoxins, and this aspect will need to be kept under surveillance if a small perceived hazard is not to be exchanged for a greater actual one.

Food Irradiation

Despite the rigorous evaluation of the safety of irradiated foods by numerous expert committees at national and international levels and extending over a period of more than 25 years—and the approval of the use of the process by a number of governments—there is still resistance to its introduction by many consumer groups. This emphasizes the need to address the social, ethical, and political aspects of food safety issues as well as communicating effectively on the purely scientific aspects.

Even at the scientific level, further research needs have been identified by the expert committees (11), and there is concern among consumers about the putting in place of adequate controls to ensure that defined, approved conditions of use are capable of being policed. In particular, questions have been raised about possible "double irradiation" of ingredients before processing and afterward in the finished product, of abuse of irradiation to facilitate the use of hygienically inferior materials, and of the need for tests to determine whether foods or ingredients have been irradiated and what dose has been applied. Concerns about hygienically inferior materials include the possibility that radiostable toxins may be elaborated before irradiation and that low counts of viable organisms do not give adequate reassurance on this point.

In response to the reaction of many consumers to the idea of irradiated foods, some supermarket chains have indicated that they will not stock such products and these supermarkets will clearly need to be convinced if the process is to succeed widely.

Novel Foods and Processes

The difficulties associated with getting irradiated foods accepted are a manifestation of a lack of confidence by the consumer that the food technologist and toxicologist are able to guarantee their safety. This concern about imperfectly understood technology also extends to other novel foods and processes.

From a regulatory point of view, there are problems even of definition of what constitutes a novel food or process so that, to date, only voluntary schemes of regulation (or none!) have been established in many countries. It is ironic that the current tentative definitions proposed by some countries (e.g., the United Kingdom (15) Table 2) would certainly have caught margarine in their net in the past, while now it has a healthy image for many people. In fact, the chemical changes accompanying hydrogenation of vegetable oils, including cis-trans isomerization and bond migration to produce "unnatural" fatty acids, have never been subjected to the same
TABLE 2. Tentative definition of novel foods and processes

"Novel foods are foods or food ingredients which have not hitherto been used for human consumption to a significant degree in Western Europe and/or which have been produced by extensively modified or entirely new food production processes."

"A novel process is a process which has not hitherto been used in the processing of foods."

* UK Advisory Committee on Novel Foods and Processes

rigorous toxicological and nutritional scrutiny that would now be required of a novel food or process. Indeed, only in recent weeks, evidence has emerged that these trans-acids may have adverse effects with regard to atherogenic risk factors.

Novel foods, such as the fat replacers, sucrose esters (typified by "Olestra"), or microparticulate protein ("Simplesse") have been considered not only in relation to any toxicological hazard which they might present, but also the nutritional sequelae which might accompany replacement of, or impairment of absorption of, essential fatty acids and fat soluble vitamins. This is an extension of the normal considerations of committees such as the JECFA to a more detailed assessment of nutritional issues; although existing principles for safety evaluation can be applied to these substances, there is a need for a closer integration of the nutritional and toxicological evaluations and a holistic approach to food safety assessment.

With regard to the products of biotechnology, the JECFA have elaborated principles for the safety evaluation of enzyme preparations used in food processing (reference 6, Annex III) which uses a five-category classification scheme to determine the extent of testing required, the least being required of enzymes (classes i or ii) derived from edible tissues of animals or portions of plants commonly used as foods; more extensive toxicological testing would be required in the case of enzymes derived from microorganisms, particularly those with no substantial history of use in food processing. An example of the latter might be a microbial rennet to be used in cheese manufacture and derived from an organism not customarily eaten in foods.

More significant problems may arise with the newer products of biotechnology, and the FAO and WHO cosponsored a meeting of experts on biotechnology and food safety in November 1990 to consider these issues. Of particular concern are the products of genetic manipulation that have a somewhat Frankensteinian image to the nonspecialist and do indeed pose new problems to the scientist involved in food safety assurance.

The United Kingdom Advisory Committee on Novel Foods and Processes has addressed these problems during its first year of operation and drafted a decision-tree approach to determining what information would be required in the evaluation of such materials (15), while the International Food Biotechnology Council is also drafting guidelines on Assuring the Safety of Foods Produced by Genetic Modification (16). The sort of information that will be sought in the safety evaluation process is listed in Table 3.

Clearly this is another area where perceptions of safety, as well as actual safety,
TABLE 3. Information needed in the safety evaluation of novel foods/processes*

1. History of human exposure (if any)
2. Probable intakes/extent of use
3. Technical details of process and product specification
4. Nutritional evaluation
5. History of organism (where appropriate)
6. Characteristics of derived strain of organism compared with parent strain
7. Toxicological assessment
8. Human data (including allergenicity, tolerance)
9. Assessment of genetic manipulation procedure (where appropriate)
10. Effect of a genetic manipulation procedure on known properties of the parent organism (where appropriate)
11. Genetic stability (where appropriate)
12. Site of expression of any novel genetic material
13. Transfer of novel genetic material to other organisms
14. Assessment of a manipulated organism for survivability colonization and replication/amplification in the gut

* From UK Advisory Committee (15).

are of importance. Further, ethical considerations, e.g., in relation to transgenic animals, mean that the debate will not center solely on safety.

“Chemicals” in Food

The significant trend against additives in food and a growing market for “organically grown” foods will be likely to add impetus to the search for alternatives that are seen as safer or more “environmentally friendly.” More specifically targeted methods of pest control, e.g., species-specific pheromone traps, may reduce the need for the more toxic and less specific pesticides. However, risk-benefit decisions will have to be made about how far this approach can be taken and, as mentioned earlier, fungicides may actually offer reduced overall health risks as well as economic benefits when properly used.

Alternative methods of processing to minimize the need for additives will also continue to be sought but, as with the cook-chill system, may raise other safety issues that need to be addressed. Novel processes will need evaluation as well as novel products.

Toxicological Methodology

The conflicting pressures of demands for increasing standards of food safety assurance and reduction in the use of animals in experimentation will continue to fuel the search for more in vitro tests in toxicology. However, there are inevitable limits to the extent to which such tests can replace whole animal studies since some adverse effects, e.g., interference in neuroendocrine control systems, cannot be simply
mimicked in vitro. Furthermore, because food safety involves nutritional as well as toxicological aspects, as seen par excellence in the evaluation of irradiated or novel foods, the need is for a more holistic appraisal.

New approaches to the evaluation of chemicals that occur in small quantities in food are needed; the nonsensical concept of testing for carcinogenicity at the maximum tolerated dose is producing more noise than light and needs to be rethought in relation to food additives. Further, the routine tests used in food toxicology need critical review because they are frequently misleading in relation to human risk. A more mechanistic approach to investigation of toxicity is needed.

Finally, there is a temptation to move toward quantitative risk assessment prematurely, giving a false sense of assurance or fear in some cases. Before this process can have any validity, in this author's view, we need a better appreciation of the mechanisms of toxicity, and the mathematical models for low-dose extrapolation need refining to reflect biological reality. Current techniques can give risk estimates varying by many orders of magnitude and these estimates are more a function of the mathematical model than the biological processes. By analogy, we may use a normal distribution function to describe the statistical distribution of, say, liver weight but we recognize the limits to its validity; the mathematics say that there is a finite probability of observing a microscopic liver, the biology tells us that this is inconsistent with survival. It is both statistically and biologically unsound to extrapolate in this way, particularly when the mathematical model is not demonstrably linked to a biological process.

Similarly, the extrapolation of toxicological results between species (to man) needs to be placed on a more secure scientific basis with greater attention being paid to metabolic and pharmacokinetic differences between species.

REFERENCES

DISCUSSION

Dr. Schifffman: How do you feel about adding chlorinated sugars to the food supply? Is dichlorofructose mutagenic?

Dr. Walker: Dichlorofructose is not mutagenic at the levels likely to be produced on breakdown of sucralose. The main problem is the finding of a condensation product with glutathione in the one-position, which has been interpreted to mean that a reactive species has been produced that reacts with glutathione. A good deal of long-term evaluation has been going on, not only of sucralose but also of obvious breakdown products. However, I still feel a little uncomfortable about chlorinated sugars.

Dr. Ashwell: Could you tell us a bit more about the use of ADI in quantitative risk assessment?

Dr. Walker: The philosophy behind ADI is that there is a threshold below which there is no manifest toxicity—the no observed effect level. Acknowledged exceptions are idiosyncratic responses, allergy, and genotoxic carcinogens. I think everyone would feel very uncomfortable about even small levels of carcinogens. However, we have to face the problem that the JECFA is called on to make evaluations of such carcinogens. How is one going to set an ADI for aflatoxins? You can say zero but that is not a practical solution—you would have people dying of malnutrition rather than intoxication. So the approach must be to accept the lowest level that is technologically achievable. Of course no one is going to allocate an ADI to an optional additive that is a genotoxic carcinogen. On the other hand not all carcinogens are necessarily excluded, if, for example, tumor production is only secondary to a hormonal effect.

Dr. Hulse: The synthesis of transgenic hybrids in which agronomically useful genes are transferred from wild into cultivated species is technically well advanced. Do we possess adequate protocols to monitor such transgenics, to ensure that the desirable genes do not carry with them substances that are a potential health hazard?

Dr. Walker: That is a serious issue. The deliberate insertion of a gene in such a way as not to express undesirable traits is more capable of rigorous control than mutagen-induced mutations. We do however need rapid nonspecific short-term tests to predict toxicity. I doubt whether such tests can be made to predict all forms of human toxicity. On the other hand evaluation by traditional procedures is very costly.

Sir Kenneth Blaxter: Regulatory mechanisms are already being put in place around the world with respect to the release of genetically modified organisms. It is correct that where techniques of gene manipulation of plants are already established, gene insertion is very well controlled with regard to release at the present time. Most of these manipulations relate to
dicotyledonous plants in which it is easy to insert genes. At present we are assessing risk and along with this there is the element of economic feasibility, as you have indicated. How far is there going to be an assessment of the overall benefit?

Dr. Walker: The mechanism for assessing benefit is not so well developed. It is difficult to develop such a mechanism unless you are willing to say that a human life is worth a certain amount of money. This is where you come across ethical and social resistance. The problem of communicating the issues about genetic research is also a very real one. The subject still tends to be dominated by the Frankenstein image.

Dr. Richardson: Some traditional methods of food preservation depend on the use of sugar and salt. Nutrition guidelines recommend reductions in these. Is there any evidence to show that the increasing incidence of food poisoning is the result of these changes in product formulation?

Dr. Walker: I don’t think so. I am more concerned about cook-chill practices. I get very worried about working women who also take care of home, who shop on their way to work and keep cook-chill food gently incubating in the back of their cars all day until they get home to prepare the food in the evening, or even hold it in the fridge for a further period. There is a good deal of information to be gotten across to the consumer yet.

Dr. Maurice: Communication with the consumer is a real problem. There is a great discrepancy between perceived hazard and real hazard. Unfortunately industry may bow to public pressure to eliminate the former while generating the latter, for example the avoidance of synthetic preservatives leading to the real hazard of mycotoxins. It seems that in general we fail with the media. How can we get it right?

Dr. Walker: There is difficulty in making an objective assessment of the information to be communicated. There is also difficulty in terms of scientific illiteracy, which gets in the way of communication. There are, however, well qualified people who can act as watch dogs for the consumers. If we were more open in our regulatory processes and in communicating the basis of decisions taken, suspicions about scientists in their laboratories would in some measure be defused. We have to be more open in safety evaluation and in regulatory processes as a whole.

Dr. James: There are real difficulties about coming to terms with current toxicological testing. Interactions between various toxins may not be examined. Single toxins are tested in animals on diets that are completely different from those likely to be used in man. Toxicological tests tend to be crude and to rely primarily on histology of different organs. How do you cope with these questions if raised by the consumer?

Dr. Walker: Not totally effectively at the moment. Increasing emphasis is being placed on pharmacokinetic and toxicodynamic aspects of safety testing, not just histology or morphology. In other words there is now an emphasis on the mechanisms of toxicity. I think this will make extrapolation more secure. However, I still see in committees that such toxicokinetic data are viewed as ancillary to histology. So far as interactions are concerned, there is increasing use of group ADIs for compounds that produce toxic effects by similar mechanisms. This is being applied to a number of food flavors, antioxidants, and so on. For interactions at the chemical level, data are now required on the stability of foods under conditions of use and on interactions with other materials. With regard to interactions with nutrition, we need to develop a holistic approach. There is an enormous variety to cover. In practical terms it is not possible to look at all possible interactions between additives or contaminants and all nutrients. By identifying mechanisms we may be able to identify more confidently those nutritional interactions that may occur.

Dr. Goldberg: The use of cell lines in toxicity testing deserves comment. Since we cannot
get primary cells for human culture experiments we have to use transformed or immortalized cell lines. These are in essence changed cells and there is no particular reason why their metabolic or regulatory processes should be the same as those in vivo. The drug or food additive that you test may not be carcinogenic in cell culture but may be changed or metabolized in vivo and the metabolites may be carcinogenic. There is a limit to how much a cell culture can tell you.

Dr. Walker: I agree. I see cell culture work as an adjunct not as a replacement, but it can be very useful in providing pharmacokinetic data.