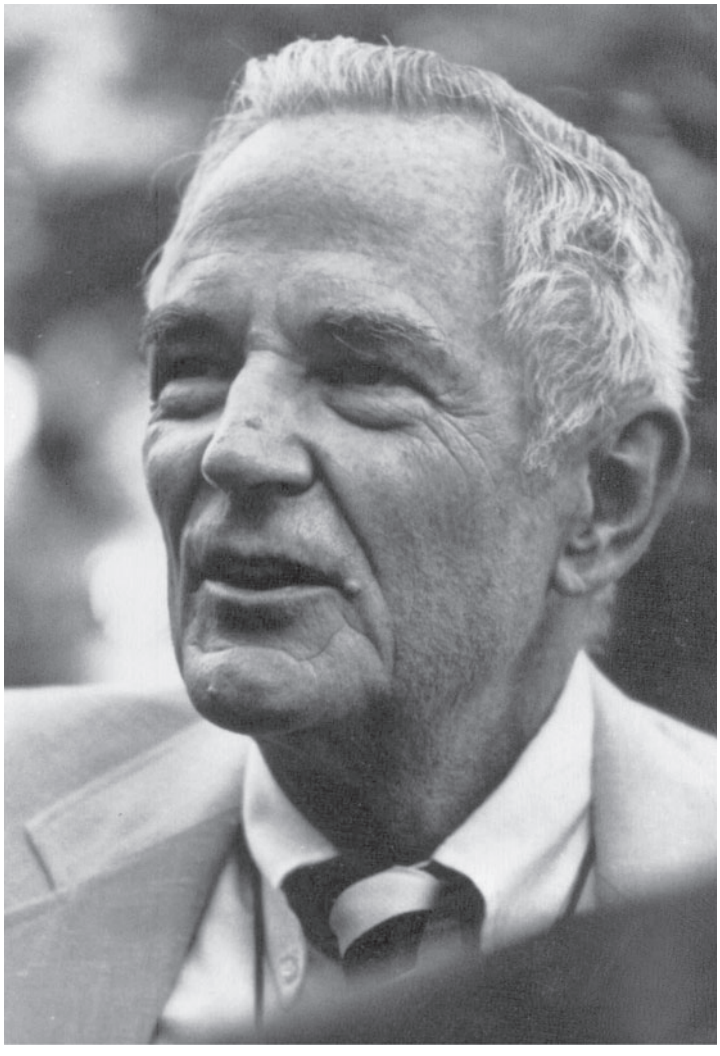

Richard Hall

Lessons Learned

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Abstract

The paper discusses my early years, education, and life experiences, including aspects of my career at McCormick & Co., Inc. A major intensive effort, one that greatly influenced my career, was helping the flavor industry cope with the passage of the Food Additives Amendment to the Food, Drug, and Cosmetic Act. It resulted in a program now in its 51st year that is unique in the food industry. Other activities took me further into the fields of toxicology, structure/activity relationships, food safety, nutrition, and biotechnology. The paper closes with some observations on current challenges, and the steps that, in my opinion, we must take to meet them.

IT WAS NOT "A DARK AND STORMY NIGHT . . ."

This is no comprehensive personal history. It is simply a record of experiences that were formative, informative, transforming, simply interesting, or some combination thereof.

Life for me began June 14, 1923, in the small town of Roseland, Nebraska. Growing up in a small town has advantages—no crime, gangs, drugs, or violence. My mother, eager to give me a head start, and skeptical of adequate rigor in the local school, taught me at home, and I entered school at the age of six in the third grade. Later, that was helpful; at the time it guaranteed that I was always the smallest boy in the class. High school was pleasant but undemanding; I do not recall any homework.

It was the Depression and the Dust Bowl, and money was scarce. I had assumed that I would work my way through nearby Hastings College, from which my parents had graduated. Our school principal, Lewis Douglas, a wonderful man, saw a flyer from Harvard announcing a very rich scholarship offering—in today's jargon, a full ride plus. Harvard, even then pursuing diversity, wanted to attract more low-income, rural, Midwestern students, and I qualified on those grounds, if no other. He urged me to apply. I thought it a fool's errand, but to my amazement and lasting gratitude I received the scholarship. It was culture shock: from a senior class of 15 to a freshman class of 1,000, from a town, population 180, to a metropolis. It was the first time that this 16-year-old had ever been addressed as "Mr. Hall." It was also a life-changer.

Harvard was an incredible opportunity and, at first, a daunting challenge. I had never really learned to study, and I spent my freshman year simply getting my legs under me. My freshman adviser was George Kistiakowsky, a famous physical chemist, later key in the Manhattan Project, and under Eisenhower, the first Presidential Science Adviser. He lunched every Friday with his advisees. I have on my wall a framed lunch menu from April 14, 1940. I keep it not to remember what I ate that day, but because the scribbling on the back begins with $E = mc^2$. "Kisty" was explaining to us the significance of the recently announced discovery of the fission of U^{235}, and on the basis of the published fission products, calculating the incredible amount of energy released, and what uses it might have. Who says it is hard to get to know senior faculty at a large university?

Senior year is a memory of rush and pressure to get through before enlisting in the Army Air Force. I became a navigator and, with our lead crew, flew 30 missions in B-l7s, mostly over Germany. The war ended while I was awaiting reassignment to the Pacific.

In the fall of 1945, I arranged to enter graduate school at Harvard. I was able to obtain posts as resident tutors in Kirkland House for myself and for Brice DeWitt, my former roommate, best man, and later a world-famous theoretical physicist. That meant free room and board and the G.I. Bill—prosperity, almost! Brice came to my room one night and proposed that, simply for fun, we construct all the regular polyhedra (solids whose faces are all regular polygons) that we could imagine. We began with the tetrahedron, cube, and octahedron, and went on from there. It took us three nights, and we finally had 18 of them on my mantle (DeWitt-Morette 2011). We couldn't visualize how there could be any more. Bryce decided to think it over; perhaps he could prove that is all there are and we could publish! He came back two days later, crestfallen. We had been anticipated by a mere 2,500 years by Plato and Archimedes. Lesson learned: Before starting anything substantial, check the literature. I still have on my bookshelf a great rhombicosadodecahedron as a reminder of that lesson.

ADDING SPICE TO LIFE

Graduate school was a stimulating experience, particularly because I did my thesis under Robert Burns Woodward, later a Nobel Laureate. My topic was an obscure aspect of the structure of

the alkaloid strychnine, then not fully known. It was fascinating and resulted in discovering a new type of isomerism. However, it was rarely useful to mention strychnine after I joined a food company. My Harvard experience was, in my mind, ideal. It was a wonderful scientific education in the context of a great liberal arts university. The most important things I carried away were (*a*) my wife, Barbara, with whom I have celebrated 63 years of marriage and counting; (*b*) awe at the extent of fascinating knowledge and dismay at realizing how little of it I could capture; (*c*) dislike of sloppy thinking; and (*d*) appreciation for the ruling importance of passion in teaching and research.

FDA: Food and Drug Administration

FEMA: Flavor and Extract Manufacturers Association of the United States

CFR: Code of Federal Regulations

R. B. Woodward's special interest was natural products, the interesting chemicals that plants and animals make as repellents, pesticides, pheromones, and pollinator attractants, among other functions. Biochemists call them secondary metabolites. It would seem natural that I would then join a spice and flavor company, but the actual reason was totally different. After the war, the pilot of our bomber crew had gone to work at McCormick and Co., Inc., and talked me into joining the firm. It was a wonderful but challenging opportunity. The spice industry goes back to Biblical times, and household extracts were hardly modern; indeed, the Aztecs served vanilla-flavored chocolate to Cortez. In 1950, the industry was still very mired in traditional practices. McCormick and Co. did not have a research laboratory, and it became my job to start one. Although I could not fully anticipate the future, the timing was fortunate. We were then at the cusp of the change from wet chemistry to modern methods of instrumental analysis, and no industry has been more dramatically transformed by instrumental analysis than the flavor industry (Hall et al. 2009).

Product and process improvement, new products, and potential substitutes in the event of another war (the Korean War was then underway) all received attention. There were some inevitable failures, some technical successes that were market failures, and some real successes.

One major problem, sadly, was extensive adulteration. When I joined McCormick, there were many so-called "pure" vanilla extracts on the retail market that had never seen a vanilla bean. The Food and Drug Administration (FDA) could not prosecute adulteration because there were no federal standards defining what vanilla should be and no effective methods of analysis. Partly through the trade association, the Flavor and Extract Manufacturers Association of the United States (FEMA), and partly in McCormick's own new research facilities, we began devising modern methods of analysis, first using paper chromatography, then gas chromatography, and ultimately, all of the modern instrumental methods (Stahl et al. 1960, Sullivan et al. 1960, Stahl et al. 1961, Stahl et al. 1962). Interestingly, some of the industry's worst offenders supported the association's methods research program. I was never sure whether they did so out of embarrassment or from a desire to keep informed about the program hoping to stay ahead of it. With increasingly effective methods in hand, McCormick applied for a Federal Standard of Identity for vanilla products, and after a prolonged intraindustry dispute, FDA issued such standards (21CFR Sections 169.175–177). In the years since, gross adulteration has virtually disappeared, and such that still exists is limited and not very profitable.

My thoughts on free markets and regulation—especially as we confront looming shortages—were strongly influenced by Garrett Hardin's seminal paper, "The Tragedy of the Commons" (1968). He used the example of a town of 200 years ago in which the inhabitants grazed their farm animals on the town commons. As the town grew, the commons could no longer support the growing number of animals. The individual resident then had a choice. He could choose not to put more animals on the common, to preserve its usefulness, or he could put more animals on to obtain a larger share of a declining resource. He would almost invariably choose the latter, forcing the town to act to prevent collapse. From this, Hardin contended that there are many large, unavoidable problems for which there are no technical solutions. Appeals to conscience rarely work. "Mutual coercion, mutually agreed upon" is the only solution that avoids eventual

ruin. The president of Harvard makes the same point in conferring the law degree. Referring to laws, he uses the phrase, "those wise restraints that make us free." Lessons learned: Science has made *caveat emptor* (let the buyer beware) obsolete. An inadequately regulated free market is an invitation to greed and fraud. A strong FDA, wise regulation, and an effective trade association are an ethical company's best assurance of a level playing field.

McCormick has grown wonderfully, and the technical departments with it. New products, improved processing, technical support, and tighter quality control were part cause, part result of that growth.

FAA: Food Additives Amendment

FFDCA: Federal Food, Drug, and Cosmetic Act of 1938

GRAS: Generally recognized as safe

IFT: Institute of Food Technologists

MOWING TALL GRAS

In 1958, after years of growing public concern, Congress passed the Food Additives Amendment (FAA) to the 1938 Federal Food, Drug, and Cosmetic Act (FFDCA). The change was overdue and largely constructive. It laid on industry the responsibility for showing an additive to be safe, rather than leaving the FDA with the task of proving it unsafe. It introduced the concept of safety in use, rather than continuing to assume an old but unsupportable distinction between absolutely safe and absolutely unsafe. Of great later importance to the flavor industry, it established the principle of GRAS (generally recognized as safe). A substance may be GRAS, and therefore not regulated as a food additive, if it is ". . . generally recognized among experts qualified by training and experience . . . to be safe under the conditions of its intended use . . .." For substances in use before 1958, that recognition could take place on the basis of "either scientific procedures or experience based on common use in food." For substances introduced later, the recognition must be only on the basis of scientific procedures [FFDCA, Sec. 201(s)].

Few sectors of the food industry were prepared to comply at once; there was only very partial general knowledge of the ingredients then in use. For our small flavoring industry the task was particularly intimidating. It became evident that our then more than 1,000 ingredients constituted more than 75% of the number of all substances intentionally added to food. There was general knowledge of most flavoring ingredients, but by no means all, and for the great majority, a general assumption of safety-in-use, but little or no organized information to support those assumptions. Simply by accident, I was chairing the then recently appointed Food Additives Committee of the FEMA. It was apparent that we had a huge and urgent task before us—to acquire the information that would permit us to be in full compliance with this new amendment. That task was to take a good part of my time and that of many others for the next eight years, and it was to change the direction of my career specialty from food chemistry and technology to toxicology and safety evaluation of food components. By far the most intelligent thing I did was to persuade the FEMA to retain Dr. Bernard L. Oser [a founding member of the Institute of Food Technologists (IFT)] as a consultant. He not only provided excellent advice, he became my mentor in this new turn in my career.

Just as we were planning how to acquire the information we needed, I delivered a paper based on what little we had learned so far. In it I attempted to lay out the problems that the flavor industry faced in complying with the FAA and what seemed to us to be the obvious approaches to dealing with them (Hall 1959). I totally failed to foresee the importance the GRAS provision would later have for the industry; indeed, I did not even mention it. In other respects, the substance of the paper correctly foreshadowed many of the principles of safety evaluation the FEMA Expert Panel was later to develop and apply. I was, however, incredibly naive in assuming that others would promptly agree with what seemed obvious to us. It took enormous work, summarized below, and six years to achieve success domestically. We have accomplished much internationally, but that is still a work in progress.

We began our information acquisition and organization task with a survey of all flavor and numerous food companies to find out, if unknown, the chemical identity or botanical source of all flavor ingredients then in use, their history of use, the levels in parts per million introduced into specific classes of final foods as eaten, and all information that related in any way to metabolism, toxicity, and safety in use. All was manual; electronic processing was years in the future. The questionnaire forms were 14 × 24 inches and the instruction book on how to fill them out was 50 pages. We placed on each questionnaire the chemical and botanical names, as well as the chemical structure of each substance, when known. All else had to be filled out by hand by each respondent. We held training sessions at trade association and IFT national meetings.

One problem was the near-paranoid attitude of the flavor industry about formula secrecy. They can hardly be blamed; formulas were, and still are, extremely valuable intellectual property, even more so before today's methods of instrumental analysis permitted substantial reverse engineering. Nevertheless, coded questionnaires and the urgent need to comply with the new legislation or lose valuable ingredients resulted in a high level of participation. Approximately 80% of the industry's use of flavoring ingredients was covered.

Tabulating the detailed results from well over a hundred companies took our committee six months of sheer drudgery, using the old mechanical calculators, unknown today to anyone under 40. Near the end, one of our members sent me a plaintive note, from Isaiah, 6:11: "I said, how long, O Lord?" Naturally I responded with the rest of the verse: "Until the cities lie waste without inhabitant, and houses without people, and the land is utterly desolate." When we finished that mind-numbing task, we had the first and only essentially complete compilation anywhere in the world of all substances then in use by the flavor industry. It was to prove exceedingly valuable.

We promptly shared the compilation with the FDA, and suggested that it could be the basis for addition of most of the covered substances to the FDA's GRAS list (currently 21CFR Subpart A, Sections 182.1, 182.10, 182.20, 182.40, 182.50, 182.60). But our list was far longer than anyone in the FDA had anticipated. Worse yet, the great majority of items lacked the typical thick file of toxicological data that the FDA was accustomed to seeing on other additives, usually synthetic and therefore less familiar, and used in far greater quantity and at far higher use levels than flavors. In effect, the agency threw up its collective hands, and the subject stalled.

After mulling over the stalemate for a few days, Ben Oser and I jointly came to the conclusion that the only way out lay in persuading the FEMA to set up a strictly independent panel of unquestioned expertise to look at the data, decide which flavoring ingredients were then GRAS, which needed more data to reach a conclusion, and which should not be used. Ben Oser served as the nonvoting chairman of the panel. McCormick was not at that time in the flavor business. Our raw materials, spices and herbs, were already on the FDA GRAS list, so I was free to serve as the panel's nonvoting executive secretary. The history of this effort, now in its 51st year, has been well recorded elsewhere (Hall & Oser 1965, Oser & Hall 1977, Woods & Doull 1991, Hallagan & Hall 1995a, Hallagan et al. 2009, Hallagan & Hall 2009). The conclusions of the panel, and the rationale for them in the form of Scientific Literature Reviews, continue to be fully published in order to reinforce an essential component of GRAS: general recognition of safety. The last reference cited above contains an essentially complete list of these publications. The result was, without our quite foreseeing it, that the FEMA became, for many years, the world's principal repository of extensive information on flavoring ingredients and their safety in use. Throughout these 50 years, the FEMA shared all data with the FDA. For me, it was a wonderful learning experience, a graduate program in toxicology without the inconvenient necessity of any undergraduate prerequisites.

Lessons learned: (*a*) Having all the information available gives one a high measure of control over one's future. It permits one to be the first to foresee problems, the first to address them, and the first to benefit. (*b*) There is no substitute for the highest level of expertise available.

(*c*) One should work with regulatory agencies and help them to be effective. (*d*) Most importantly, common efforts can achieve results far beyond the reach of any individual or company.

POTPOURRI

Although my involvement in flavors and their safety continued (Hall 1981b, Munro et al. 1998), my interests broadened. A most instructive experience was serving as a member of a Panel on Chemicals and Health under the President's Science Advisory Committee. The committee existed until President Nixon received so much advice he didn't like that he abolished the committee. For more than two years we met monthly to learn about almost every conceivable use of, or exposure to, chemicals. We learned about prescription and over-the-counter drugs, food additives and residues, the composition of detergents, cosmetics, pesticides, effluents, byproducts, and much more. The issuance of our report (President's Science Advisory Comm. 1973) was delayed because it was on Haldeman's desk when Watergate struck. Obviously, we wondered if we had been recorded but concluded that we really weren't that important.

In 1967, I was asked to chair the organizing committee for the Third International Congress of Food Science and Technology to be held in Washington in 1970. It was my first major venture into international science. It provided a much-extended view of our professional field. It led eventually to my becoming president of the International Union of Food Science and Technology, to wonderful experiences, and to many warm friendships around the world.

The summer of 1972 provided a curious experience. Earlier that spring, Nixon's presidential science advisor suggested that it would be appropriate, popular with the scientific community, and good politics for the upcoming election to announce a series of Presidential Prizes for Innovation. They were not simply for a promising new idea but for a new idea that had been put into practice with obvious public benefit. It was all very rushed; most of the hundred or more nominations were hastily and inadequately done. A task force of government scientists had sifted through them and helped the nominators improve the more promising ones. An outside jury consisting of 14 assorted other individuals and me was somehow selected to go over the survivors and make a semifinal choice of from 5 to 15, from which the president would then make a final choice. We were given only a day and a half. We spent the first afternoon wondering how it could possibly be done; how could one possibly rank for innovative merit nominations as diverse and dissimilar as Sesame Street, Fortran (an early and groundbreaking computer language), the artificial kidney, and a deep sea oil rig that, even if swept away by a hurricane, could find the same drill hole? "Apples and oranges" seemed easy by comparison. But, somehow, on the second day it all began to gel and we had little trouble settling on 15. We had been cautioned to be silent; we had done our job and then, oblivion. Almost two years later, the director of the National Science Foundation (NSF) announced that the program was dead. Someone (not I, no Wikileaks fame for me!) leaked a generally accurate version of the story to *Science* (Shapley 1974). Apparently, there was some resistance from the NSF, fearing that the prizes would compete for attention with the National Medal of Science. I also suspect it was another casualty of Watergate.

It was an interesting experience for what it revealed about the present state of technology. Two obvious aspects were true of all our 15 finalists. There was, of course, the imaginative leap, the new and improbable concept. There was also, in every case, someone or several someones who were so totally convinced of the merit of that concept that they pursued it tirelessly against strong, widespread disapproval. The third, and more discouraging, aspect was that in 13 of the 15, the proponents ultimately had access to high levels of external financial support, or they could never have persisted to success. There were two exceptions. One was a retired professor of mining engineering. He was convinced that he had a way to extract useable iron ore out of taconite, a

low grade ore of which there are ample supplies. It required grinding the taconite very finely, then separating the iron magnetically. He had no resources, but he would make the rounds of the facilities where his former students worked. He would borrow their pilot plant for a day, then go home and analyze the results. This continued for years until he succeeded. The other exception was the inventor of several electronic devices, including the mercury battery, but he was a self-taught electrical engineer and wealthy inventor. Lesson learned: The path to a successful major innovation is long, hard, and expensive.

NUDs: Natural or unavoidable defects

In the 1970s, I became increasingly involved in other aspects of food safety and quality (Hall 1978, 1979, 1997, 1999), including natural toxicants (Hall 1973b, 1977) and novel foods (Hall 1986). It struck me very forcibly that public concern was racing far ahead of public knowledge and that professional societies needed to take an active role in public education (Hall 1971, 1973c). When serving as IFT president in 1970 and 1971, I appointed IFT's first Expert Panel on Nutrition and Food Safety, and with it, the first set of regional communicators, now science communicators, who were to be IFT's contacts with the local media. A few of my colleagues thought that unfortunate; we were a scientific society and should not get involved in public controversy. Happily, this view soon disappeared. Also beginning in the 1970s, my activities in toxicology and safety evaluation expanded to include areas other than flavors and GRAS (Hall 1973c, 1984b, 1985, Hall et al. 1989, Hall & Taylor 1989).

THINGS NO ONE WANTS TO KNOW

Spices and herbs are products of nature. Herbs are the aromatic leaves and flowering heads of plants of temperate origin. Spices, narrowly defined, are the aromatic bark, fruit, buds, or leaves of plants of tropical origin, and that origin is frequently in areas not noted for high standards of sanitation. Thus, they come endowed with all the contaminants that an ingenious nature can provide—often, a significant bacterial load, as well as insects and unpleasant residues of higher forms of life. The FDA recognizes reality and publishes defect action levels for these problems; with admirable tact they call them natural or unavoidable defects (NUDs). The defect action level is the level at or above which the FDA would take regulatory action. The spice industry has long struggled to reduce or eliminate these problems by improved sanitation at the source, better postharvest handling, and a variety of methods for removing what problems remain. Fumigation and cleaning to remove insect contamination are major tools.

We at McCormick would occasionally receive, not a complaint about one of our products, but a generic complaint, "Why does your industry permit such filthy products to go out on the market?" I would send them a calm response explaining the inevitability of some contamination and describing in more detail than they wanted to know all of the measures we took to minimize and eliminate it. Approximately 40 years ago, for reasons now forgotten, the spice industry received a growing blast of publicity about contaminated spices. The peak was a front-page article in the *Wall Street Journal* headlined, "Does Your Paprika Get Up and Walk Away?" At that time, the FDA's defect action levels for NUDs were unpublished, partly because the law unrealistically holds that no contamination of any kind is permissible. The FDA was under growing pressure to make public the levels on spices. I then made one of the only two requests I have ever made to the FDA. I called Virgil Wodicka, head of the then Bureau of Foods, and asked that if they publish the defect action levels, do so not just on spices, but publish them on all foods. He assured me they would publish all, and they did (FDA 1998). The public then realized that there were thrips in sauerkraut, insect eggs and maggots in tomatoes, and rodent hairs and insect fragments in all of a long list of foods of plant origin. We never received a single generic letter after that. Lesson learned: It is possible, although sometimes painful, to educate the public.

BENEFITS AND RISKS, PERCEPTIONS AND MISPERCEPTIONS

In the early 1950s, we at McCormick began investigating irradiation as a possible tool in this effort to deal with contamination. It would not be cheap. Fumigation and cleaning were effective and far less costly than irradiation for insect removal. The only method then available for greatly reducing the bacterial load was fumigation with a gas, ethylene oxide. It was a dangerous substance, having the widest known explosive range in air—from 3% to 100%. Even a modest knowledge of structure/activity relationships would mark it as a potential carcinogen, as indeed it turned out to be. We dealt with the problem by developing proprietary methods of reducing microbial populations and renewed our earlier interest in irradiation (Hall 1984a, 1989a). In 1985, I delivered an unpublished paper at a meeting in New Zealand that reviewed all published tests on the safety of irradiated foods. It concluded that all tests showing adverse effects were deeply flawed or unconfirmable. Common sense and early testing suggested that if any harmful products of irradiation (radiolytic products) occurred, they would be present only at very low levels and their effects would be difficult to detect. Absent a knowledge of mechanisms, toxicology's only weapon for detecting small effects is to increase their probability by increasing the dose. However, greatly increasing the intake of any single irradiated food inevitably results in distorted diets and seriously adverse nutritional effects. If the control diet consists of the same intake of the same unirradiated food, similar adverse effects are observed. There were few properly controlled studies, and those few showed no ill effects due to irrradiation.

We filed petitions for the use of ionizing radiation on spices. The FDA eventually published regulations on spices, and later on a wide variety of foods (21CFR Sections 179.21–179.45). In spite of further extensive testing that has assured safety, and strong support from public health agencies seeking to reduce food-borne disease, irradiation of food has not become common in the United States. In part, that is the result of uninformed—or misinformed—public resistance, a fear of anything with the words radiation or nuclear attached. In part, it is because we have several effective processes long in use that make investment in an expensive new process unattractive. Curiously, the same people who fear irradiated food receive without concern joint implants and sutures that are radiation sterilized, as is the equipment through which they receive intravenous medications (Floros et al. 2010).

From time to time, I became involved in the interesting area of food acceptance (Hall 1958, 1981a, 1987). From a variety of experiences, especially those involving risk and safety, it was logical to have an increasing interest in risk/benefit considerations (Hall 1973a, 2006; Bidlack et al. 2009). My thoughts about risk/benefit were greatly influenced by a provocative paper by Chauncey Starr (1969). He estimated the perceived difference in acceptability between voluntary and involuntary risks by observing how much people are prepared to pay to accept or avoid them. Using many examples, he estimated that consumers are 1,000 times more willing to accept a voluntary risk—one over which they feel they have control—than an involuntary one. That has obvious applications to food. Obesity is a voluntary risk; pesticide residues and environmental contaminants are not.

Experience with intake calculations led to involvement in nutrient and flavor intake estimation (Beaton et al. 1988, Hall & Ford 1999), and later, to nutrition labeling (Merrill et al. 1990).

CHEMICAL STRUCTURE AND BIOLOGICAL ACTIVITY

Because extensive toxicological data existed only on a few of the most-used flavoring ingredients, the FEMA Expert Panel found, early in its deliberations, that metabolic data showing ready

conversion to common, harmless, and easily eliminated metabolites often permitted a conclusion of safety in use if the levels of intake were sufficiently low. This led to the recognition that other substances of closely similar structure would be metabolized in the same way, permitting the same conclusion. The panel came to make much use of such structure/activity relationships. In the mid-1970s, at one of the FEMA's annual meetings, Dr. Horace Gerarde, an even more remarkable member of that remarkable panel, reviewed some of the panel's activities and discussed the use of structure/activity relationships. As I sat listening to that presentation (several years after I had ceased to be the panel's executive secretary), it struck me that it ought to be possible to organize these useful tools in some more generally applicable way.

In the early 1970s, monosodium glutamate (MSG) and the artificial sweetener cyclamate, both originally on FDA's GRAS list, became the victims of poorly done, or misinterpreted, but highly publicized research and, therefore, of public apprehension. Although the details are beyond the scope of this essay, they resulted in then President Nixon ordering a review of the GRAS list. Obviously, the agency turned to the FEMA to compile the information on flavoring ingredients. Employed at that time by the FEMA were Dr. Richard A. Ford, my successor in service to the panel, and Dr. Gregory Cramer, then working to compile data for the FDA's GRAS review. I discussed with them my thoughts about pulling together in a coherent way the then-existing knowledge of structure/activity relationships and toxicological data in an attempt to create a tool for predicting safe levels of intake. To achieve credibility, it would have to cover all chemical compounds, not just flavors. We would not attempt to predict toxic endpoints, even today a challenge, but instead, realistic, useful intake levels that would be assuredly safe. We agreed to try. Greg Cramer and Dick Ford did nearly all of the drudgery of searching the literature, then done by hand. Online was not yet a concept, much less a reality. I had been impressed by the use of a decision tree key used in a tree identification book (Harlow 1957), and we decided to use a similar approach to organize our material. It took us almost three years of literature search, discarding data from shoddy tests (there was much of that), and endless tries to devise a product—a sequence of questions nearly all about chemical structure—that produced conservative, consistent, useful results. It permitted classification of any organic or organometallic compound into one of three classes of presumptive toxicity and, from the lowest-no-adverse-effect level, a prediction of a safe level of intake (Cramer et al. 1978).

The paper's reception by the toxicological community was a study in the acceptance of a new concept. Outside the drug field, few toxicologists had used structure/activity relationships to the extent used by the FEMA Expert Panel. Usually they didn't need to, and they were deeply skeptical of them. Their attention was customarily directed to a mass of conventional acute, subchronic, and chronic toxicity data. In contrast, we three authors carried the organic chemist's firm faith that of course chemical structure determines biological activity. In nearly every case, the reception went through the phases of (*a*) outright skepticism, often impatiently expressed, (*b*) reluctant consent to waste time trying it, (*c*) surprise that it seemed to work, and (*d*) gradual acceptance.

Our paper gained much further traction in 1996 when Munro et al. published an exceedingly useful paper that used our decision tree to separate into the same three classes of presumptive toxicity large databases of toxicity information that had not existed when we wrote our paper. Of various structure/activity schemes then available, only ours permitted clear separation into classes. That larger base of toxicity data then available permitted the calculation of "thresholds of concern" below which there was high assurance of safety. At last count, our paper has been cited 125 times. It is still being cited and used today, 33 years after its publication. Lesson learned: The more novel the idea, the slower the acceptance. Be patient! However, once achieved, acceptance can be long lasting.

EXPLORING UNKNOWN TERRITORY: BIOTECHNOLOGY AND SAFETY

Interest in biotechnology began to build in the late 1980s, and with it, two concerns, both understandable. First was the usual worry over anything new, especially if it has to do with food. Food, after all, is a "gut issue." Second was the realization that for once, we might get ahead of consumer concern and establish, with wide participation, procedures for assuring the safety of foods produced by biotechnology that would thus calm or prevent public concern. Twenty-six companies joined in an effort to accomplish this by forming the International Food Biotechnology Council. I was about to retire from McCormick and agreed to chair the effort. We succeeded in recruiting wide expertise from the nascent but talented biotechnology industry, the food industry, the food and drug bar, and university experts in plant breeding, molecular biology, and food safety. Our early meetings were instructive; it was clear that those of us from the food industry knew next to nothing about the methods and potential of biotechnology and equally clear that those in the biotechnology industry had given little or no thought to issues of safety. They had simply and incorrectly assumed it. It was a process of mutual education. That process, along with construction of a first draft. required almost two years, and only the invention of fax machines permitted that. We then sent that draft out for comment to scientific organizations, affected industries, consumer groups, and governmental agencies across the world. We received extensive and helpful comments, although nothing from consumer groups, but we had to ask. It was an unusual situation. A friend with Health Canada commented that, "Usually governments propose and industry comments. Now industry is proposing and governments are falling all over themselves to comment!" Our report (Caddow et al. 1990) was the first such publication, and was, as we had hoped, influential in affecting later national and international regulation. Among many others, I made efforts to publicize and extend the application of the report (Hall 1991, 1992; Hallagan & Hall 1995b). Surprisingly, in this technology, the United States has made far more use of it than most other countries, whereas the United States has not been in the lead in adopting irradiation and aseptic packaging. Lesson learned: It does help to get there first.

FEEDING TOMORROW (NEW NAME OF THE INSTITUTE OF FOOD TECHNOLOGISTS FOUNDATION)

One of the frustrating but common public misconceptions is infatuation with the "natural" as being in some way safer, healthier, better, more nutritious. Thus, I enjoyed serving on a study that resulted in a report, *Carcinogens and Anticarcinogens in the Human Diet* (NRC 1996). We concluded, to no one's surprise, that although more data are desirable, natural carcinogens in the diet are far more numerous and generally at least as potent as the few known to be of human origin. None, however, presents a significant risk in American diets, although that is by no means true in developing countries. Sadly, consumers waste much money in pursuit of the natural, unaware that much that is called natural would not meet their innocent expectations. There is a wonderful discussion of this, although with many digressions, by Hoffmann & Schmidt (1997).

On our bookshelves are many reports intended for public use to which I and many other more talented people have contributed. Their content is substantial and useful. Unfortunately, most of them have sunk without a trace. I reluctantly conclude that most reports are a waste of time unless there exists a permanent structure, such as IFT's Science Communicators, for continuing to keep their content before the media and the public.

The arguments over food irradiation and biotechnology are simply recent examples of an age-old conflict. That is the tension between the priest and the prophet, the conflict between

the defender of traditional practices and beliefs, and the ardent apostle of the need for, and the benefits of, change. There is no quick solution to this. It requires talking it through with patience and with sound information.

Continuing that thought, it is clear that we have far to go in advancing public understanding of science and its products. That task is made more difficult by our appalling lag in education in science and mathematics, and this is no time to say "We can't afford it." Those in the media are rarely intentionally misleading, but alarm sells. It is not enough to produce data, products, and technologies. We must take a far more active, accurate, and dispassionate role in reaching a level of public understanding that precludes unfounded concerns, while encouraging broader understanding of the risks and benefits inherent in all we do. An excellent recent editorial in *Science* makes these same points (Reddy 2011).

We face huge and unavoidable problems, problems that are not evenly distributed around the world. Among them are climate change, increasing water shortages, soil and environmental degradation, population growth well beyond the resources to support it, and depletion of many of the resources on which our societies are built. The science and technology to deal with them are available or within reach. But Garrett Hardin was right. There are problems technology cannot fix. It can give us the means to deal with problems, but it cannot give us the will to deal with them. That will requires, first of all, recognizing their existence rather than denying or ignoring them. It requires the ingenuity we certainly have and the freedom and encouragement to apply that ingenuity. But it requires more. Unregulated free enterprise is wonderfully effective at using what is available. Absent tax incentives or regulation, there are few large-scale examples of free enterprise conserving, restoring, or replacing. We do it as individuals; it is far more difficult to accomplish it as a society. Independent initiatives frequently result in competitive disadvantage. Thus, we require incentives. Incentives are not free; we all pay for them. It also requires the "mutual coercion mutually agreed upon" of which Hardin wrote, or, in the less aggressive language cited earlier, "those wise restraints that make us free." I hope we will have the wisdom to employ them—in time.

Nothing discussed here would have been possible without the dedicated efforts of hundreds of talented and energetic collaborators, and I owe everything to them. The IFT has been my principal professional society, and I am grateful to my fellow members and its dedicated staff for all the help, encouragement, and opportunity they have provided. History of all sorts has always held my interest, and when IFT was preparing to celebrate its 50th anniversary in 1989, I gladly accepted an invitation to prepare a brief review of the Institute's founders. It was a fascinating and rewarding task (Hall 1989b). I cannot close without thanking my wife, Barbara, whose patience during my many absences was, in retrospect, astonishing. I must also thank my employer, McCormick & Co., Inc., for allowing and supporting such free-ranging activity. And, although I hope I am far from being in extremis, I can agree warmly with the last words of Lady Mary Wortley Montagu, "It has all been very interesting."

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