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The Importance of Self-Regulation in the Fragrance and Flavor Industry Views of the U.S. Food and Drug Administration

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Forces of Change

Your industry is special. It's special because of its truly interdependent and international character. It's special because of its historical origins—the role it's played through time in expressing culture and in enriching human lives. And it's special because of its diversity—from the small farmers who supply raw materials from all corners of the world, to the major companies who use flavors and fragrances in their products. These special qualities make your industry sensitive to change. And today your industry faces a period of major transition—a period of enormous scientific advances and increased global interactions.

In this respect, we share a common bond. The government agency I lead also is experiencing the pressures of change. Both face similar challenges: unleashing the promise of science, smoothing the way for international trade, assuring safe and wholesome products, and maintaining consumer confidence. Effectively meeting these challenges will require diligent efforts from both government and industry, but by working together, we can assure safer and better products for the marketplace and bring about an improved quality of life.

Keeping in mind our shared purposes, I want to discuss with you today the role of the Food and Drug Administration in regulating flavors and fragrances in the United States. I also would like to address the growing importance of international cooperation in regulatory matters.

Opportunity for Cooperation

Flavors and fragrances are regulated under the United States Food, Drug and Cosmetic Act. This law offers outstanding opportunities for government-industry partnerships in assuring safe products. It also provides the opportunity for limited government involvement when industry acts responsibly.

This is particularly true for fragrances which are regulated under the cosmetic provisions of the Food, Drug and Cosmetic Act. This law prohibits the distribution of cosmetics which are harmful or whose label is misleading. It does not subject cosmetic products to a pre-market approval process as required for many other articles that fall under FDA's jurisdiction. And it does not require that individual fragrances be disclosed in labeling.

This legal and regulatory framework for fragrances underscores the need for effective self-regulation by the suppliers and manufacturers of fragrances. With freedom, comes the challenge of responsibility. Here in the United States, we have been impressed by the quality of scientific efforts your industry has supported to meet this

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challenge. FDA has had a long and productive relationship with the fragrance and flavor industry. We appreciate the magnitude of your task in developing a system to address the many thousands of ingredients used by your industry in consumer products.

Work of RIFM and IFRA

The fine work and leadership of the Research Institute of Fragrance Materials (RIFM) and the International Fragrance Association (IFRA) deserve special recognition for their efforts to assure safety. The work of RIFM in gathering scientific information, conducting tests, and evaluating the safety of fragrance ingredients is a valuable service to the public, your industry, and FDA.

The efforts of IFRA to bring self-regulation to your industry are equally noteworthy. The Code of Practice published by IFRA to promote good manufacturing practices and provide guidelines on the safe use of fragrance ingredients is a commendable voluntary effort that I fully endorse. A key element of this code is the recommendations established for individual ingredients which may potentially cause harm.

The IFRA guidelines challenge both industry and FDA to assure that potentially harmful ingredients identified by RIFM are not used in products under conditions that might harm consumers. Clearly, if such guidelines are followed, there will be less need for FDA to prohibit or restrict certain ingredients by regulation. At FDA, we have been keenly interested in the work of RIFM and IFRA and the extent to which individual fragrance suppliers follow voluntary industry guidelines.

Survey of Compliance with IFRA Guidelines

Today, I would like to share with you some preliminary findings from an on-going study being conducted in FDA's Division of Colors and Cosmetics. Under the able leadership of its director, Heinz Eiermann, and its associate director, John Wenninger, this division has been undertaking research and developing analytical methods to identify potentially harmful ingredients in fragrance preparations. During the past year, it conducted a survey of hundreds of domestic and imported finished fragrances for eight selected ingredients of toxicological interest. Although the results are still being compiled, I can give you a report on the initial findings. The survey revealed that, in general, there was very good compliance with IFRA guidelines for most fragrance ingredients included in the survey. The notable exception was musk ambrette which was found in over 40% of the products analyzed. This ingredient is a potent photocontact sensitizer, and its presence in products is a concern to the agency.

Your efforts at self-regulation have been commendable. Full compliance with IFRA guidelines is a goal you must continue to pursue. I encourage IFRA and others to continue seeking effective ways for communicating their guidelines to members of the fragrance and cosmetic industry. And I also encourage expansion of your efforts to consider more fully the question of likely systemic effects and other health implications which may arise from long-term exposures to fragrances.

Cosmetic Program Oriented Toward Research and Monitoring

As you can see, our cosmetic program at FDA is strongly oriented toward research and post-market surveillance. I'd like to call your attention to the most recent issue of one of our publications, the November *FDA Consumer*. It reports on a study sponsored by FDA showing that fragrance ingredients headed the list of cosmetic ingredients causing allergic reactions. The article is based on work done by a group of dermatologists particularly interested in contact dermatitis. The

results of this work appear in a paper in the December 1985 issue of the *Journal of the American Medical Association* entitled: "A Five-Year Study of Cosmetic Reactions." I invite you to read the *FDA Consumer* to understand consumer concerns more fully.

In other cosmetic work at FDA, we are exploring ways to strengthen our efforts to maintain a data base on cosmetic ingredient formulations and adverse reactions. And we also are undertaking biological studies which recognize skin as an important route of entry into the human body. We are actively seeking to understand not only contact sensitization but also skin penetration and skin metabolism, as well as the potential for systemic harm from absorbed ingredients. All of our efforts support the goal of regulation based on the best possible science.

Regulation of Flavors

Those of you familiar with U.S. food law know that the regulation of flavors is somewhat more complex. Flavoring materials can fall into several different legal categories. One of these, known as "food additives," requires premarket safety review and approval by FDA. Another, the "Generally Recognized as Safe," or GRAS category, requires general recognition of safety by experts qualified by scientific training and experience to evaluate the substances on the basis of scientific data derived from published literature.

Self-regulation Through Implementation of GRAS Concept

Through the GRAS provisions of the food law, the flavor industry also has undertaken vigorous efforts at self-regulation. The Flavor and Extract Manufacturers Association (FEMA) has implemented the GRAS concept in a responsible manner by convening expert panels to evaluate the GRAS status of flavoring substances. The cooperation of FEMA in identifying flavoring substances, surveying toxicological data, and developing scientific literature reviews has been greatly valued by FDA over the years. Given the limited resources of government, FEMA's activity in monitoring its industry and a vast inventory of over 1400 flavoring substances has represented an important supplement to FDA's own activities in assuring a safe food supply.

The contributions of FEMA to research—such as efforts sponsored at the University of Georgia and the Monell Chemical Senses Center at the University of Pennsylvania—also are important

to strengthening the science base supporting our knowledge of flavors. FEMA is to be commended for its efforts and initiative in support of science.

Integration of Data into Priority System

FDA has integrated data supplied by FEMA—including its most recent submissions, FEMA GRAS Lists numbers 13 and 14—into the agency's project known as the Priority-Based Assessment of Food Additives. This project is an automated data base constructed to provide a continuous overview of all potential safety concerns which might require more thorough safety reviews by the agency.

The review provided through the priority system indicates that, to date, the flavors, as a class, generally represent low potential for risk. This finding results largely from the generally low exposure for individual members of the flavor class, and the important weight given exposure estimates in the priority system.

General Trends in Safety Assurance

The Priority-Based system represents just one of the ways FDA is responding to changes in technology, science, and social concerns. But the agency also is addressing other areas, and I'd like to mention three of those now. They are risk assessment, biotechnology, and quality control.

Risk Assessment. An explosion in scientific knowledge is confronting regulatory agencies with new realities: more carcinogens are being found in smaller quantities; natural hazards from the food supply are being recognized; complex biological processes are being more fully understood; and the relationship between nutrition and toxicity is gaining more attention. These developments are forcing questions about the scientific wisdom and practicality of viewing safety in terms of absolutes. They are dramatically pointing to the need for effective means to discriminate among risks—to focus resources on those situations of greatest public health concern, rather than on the trivial, or (in legal terms) *de minimis* situations.

In response to this need, FDA has continuously refined its risk assessment strategies as a component of its safety judgment process. Increased availability of analytical methods and better scientific data have made it possible to estimate an upper limit of risk useful in making regulatory decisions. In using risk assessment, our goal is to evaluate safety in a rational, orderly fashion, taking into account relevant factors including use and exposure, I'm sure you in the flavor and fragrance industry can appreciate that a risk assessment for a compound used as a flavor ingested orally could lead to very different results from those for the same compound used as a fragrance, where factors such as the amount applied, the surface area of application, the amount absorbed and, perhaps, skin metabolism, come into consideration.

To be useful and acceptable, risk assessments must be based on the best possible science. To assure that this is the case, we are taking a number of steps at FDA to increase confidence in our risk assessments and strengthen the scientific base upon which they are founded. One of these—which I view as very important for conducting careful, science-based risk assessments—is our use of panels of experts to peer review selected risk assessments presented to the agency. One example of this use is the FDA-sponsored panel on color additives, chaired by Dr. Ron Hart of FDA's National Center for Toxicological Research. This panel conducted a peer review of risk assessments presented to FDA for three color additives proposed for external use in cosmetics. The results were published in June 1986 in the paper entitled: "Final Report of the Color Additive Scientific Review Panel," *Risk Analysis* volume six, page 117. Careful internal deliberations by FDA and external review as in

this case can provide an extra measure of public confidence regarding the products involved.

Research Needs. Because of its commitment to safety, FDA also is taking a hard look at research needed to resolve some of the uncertainties in risk assessment. We have formed a policy committee to examine the assumptions underlying risk assessments. This committee already has completed an inventory of ongoing research and now is examining the role of peer review in the risk assessment process.

We also are looking forward to opening a new research facility in 1987. Dr. Sanford Miller, Director of FDA's Center for Food Safety and Applied Nutrition, has been leading aggressive efforts to integrate food science research. Our new laboratory will allow us to bring together scientific disciplines such as toxicology, microbiology, and nutrition in exploring a new world of food science from a new perspective. It will enable us to undertake studies in pharmacokinetics and other areas, so that we can move toward obtaining more reliable and realistic estimates of risk.

Biotechnology. Integration of scientific understanding also will be needed by both industry and government if the full promise of biotechnology is to be realized. Here in the U.S., the White House Office of Science and Technology Policy has established a Biotechnology Science Coordinating Committee to promote cooperation within the government and to identify significant gaps in scientific knowledge. As Commissioner of FDA, I am a member of this group, along with other senior government officials from major regulatory agencies.

The committee has concluded, as we have at FDA, that products derived from the new biotechnology do not need to be regulated differently from those produced in other ways. The policy statements of the committee were published in the June 1986 *Federal Register*, beginning on page 23302. FDA's premarket approval reviews will continue to address products on a case-by-case basis.

GRAS Status and Biotechnology. We are often asked whether a food substance (including microbes) that is GRAS can lose its GRAS status solely because it was produced or modified by new biotechnology. The answer is "yes" if the substance and its contaminants have been altered in such a way that it can no longer be generally recognized by qualified experts to be safe. In this instance, the substance then would be a food

additive, and the portions of FDA's law and regulations relevant to food additives would apply.

Whenever a new method is used to produce a substance added to food, whether that method involves biotechnology, or some other technology, FDA believes it is important to evaluate whether new procedures change the identity of an ingredient, introduce new or altered levels of impurities, or affect dietary exposure in a manner not supported by available safety data.

This past March, FDA filed the first petition for the use in food processing of an enzyme produced by recombinant DNA techniques. The petition requests the use of alpha-amylase derived from *Bacillus stearothermophilus* and cloned and expressed in *Bacillus subtilis.* The agency is now in the process of evaluating this petition.

Whether through plant cell or tissue culture, genetic manipulation, enzyme modification, or other techniques, biotechnology offers a host of opportunities to the flavor and fragrance industry. When I visited Bio Fair Tokyo '86 in Japan, I was very interested to learn of some of the work in progress for applying biotechnology to commercial uses, including the production of lipstick color.

As the trade literature indicates, much of the interest in this new technology comes from the market for "natural" products. We must be careful, however, that we not assume that natural ingredients are inherently safer than synthetic ingredients. We know that nature can serve up toxicants such as aflatoxin and microbiological contaminants. And we know that the Expert Panel of the International Fragrance Association has warned against allergens and photosensitizers that include both natural and synthetic ingredients. Product safety—no matter what the source—is our primary concern.

I might add at this point that FDA is aware of FEMA's efforts here in the U.S. to examine the regulations defining "natural" flavors. We will be watching this exercise with careful interest.

Quality Control. Quality control is another area of vital interest to FDA. Quality control is an essential determinant of safety—the safety of raw materials, the safety of a fragrance or flavor compound and, ultimately, the safety of consumer products. Without quality control, unwanted contaminants or formulation errors may introduce potential hazards to consumers.

We at FDA recognize the important steps taken to assure quality control through the guidelines and codes of practice established by IFRA, the Food Chemicals Codex, and the International

Organization of the Flavor industry. The good manufacturing practices guidelines developed by the cosmetic industry as a self-regulatory effort; FDA's guidelines developed for our inspectors to conduct effective inspections of cosmetic manufacturing establishments; and FDA's recently updated good manufacturing practice regulations for processing and controlling the quality of food may serve as good examples to your industry for preparing your own, detailed "what-to" and "how-to" guidelines.

FDA stands ready to work with industry in the important area of quality control. At FDA, quality control remains a major concern as we examine ways to respond to new technologies, such as the growing use of computer process control in food processing and packaging. These emerging systems provide new challenges to us in developing inspection programs.

Microbiological contamination is a special concern to FDA. We also are carefully examining the issues associated with the Hazard Analysis Critical Control Point approach (HACCP), particularly for controlling microbiological hazards in foods. The goal of this concept is to focus attention on those points in a process that directly affect quality and safety.

At present we are considering whether such a system can permit FDA to make better use of its inspection resources. We also are examining whether changes in regulations will be needed. Given the complexities of today's science and technology, we want to be certain that such a process will make safety assurance more efficient and more effective.

In a related activity, FDA and the United States' Department of Agriculture are developing a plan for establishing a Commission on Microbiological Quality Standards for Foods, as recommended in a report by the National Academy of Sciences. A major objective of this commission would be developing microbiological criteria for foods when they are appropriate.

International Efforts

I'd like to turn now to the subject of international cooperation in health and safety assurance. As I travel about the world and assume my duties as U.S. representative on the executive board of the World Health Organization, the realities of our global economy grow more apparent. As markets become global, so must our approach to safety concerns. As United States' Commissioner of Food and Drugs, I am dedicated to ensuring that imported products meet United States safety and legal standards. Between fiscal years 1983 and 1986, we've increased our inspectional and analytical operations twenty percent each year. However, I also recognize the importance of harmonizing international standards to promote free trade and bring safe products of high quality to the world's consumers.

To this end, FDA is working on several fronts. FDA negotiates bilateral agreements with colleague agencies of other governments. It also is active in numerous international meetings such as this one and last year's Inter-American Food Protection Conference. And we are proud of our role in international cooperative efforts such as the development of scientific principles for overseeing biotechnology undertaken by the Organization for Economic Cooperation and Development. Our agency also participates in sharing and collecting information. And each year we play host to over two hundred scientists and officials representing more than fifty countries who visit our agency.

Some of our most vigorous efforts are through international organizations such as the Codex Alimentarius Commission established by the Food and Agriculture Organization of the United Nations and the World Health Organization. Over the years, this commission has worked successfully to protect the health of consumers around the world and to facilitate international trade. FDA is pleased that many of its scientists, including Herb Blumenthal, John Modderman and Sam Shibko, have been invited to serve as expert members and advisors—independent of the FDA—for the highly respected Joint Expert Committee on Food Additives which advises the commission. We also are pleased that Dick Ronk, Deputy Director of the Center for Food Safety and Applied Nutrition at FDA, heads the U.S. delegation to the Codex Committee on Food Additives.

Codex Activities Involving Flavors

As many of you know, this committee now is involved with two activities of special interest to those who produce and use flavors. The first of these is the "Proposed Draft General Requirements for Natural Flavorings." This document applies to natural flavorings intended for use in the preparation or manufacture of food including natural flavorings sold by retail. Thermal process flavorings are excluded in the document. At its 18th session, the Codex Committee on Food Additives agreed to follow the Codex Step Procedure for elaborating the "General Requirements for Natural Flavourings." The document currently is at Step 3 of the Codex process and has been submitted to interested governments and international organizations for comment. In

the U.S., our delegation is working with U.S. industry groups to develop a reply. Under the rules of the Codex Committee, those of you interested in commenting on this document also should work through the Codex delegations in your countries and international trade organizations.

The second activity I'd like to mention concerns the international safety review of flavors. For some time, many in the international community have been interested in an orderly review of flavors targeted efficiently to protecting public health. In 1985, the Codex Committee on Food Additives agreed with its Working Group on Flavours that the question of priority setting and consideration of flavoring substances should be undertaken by an FAO/WHO Group of Experts especially convened for this purpose. The Committee also indicated the first priority should be given to artificial flavors.

While this issue is under consideration by WHO and FAO, the U.S. delegation and members of the U.S. flavor industry have been working together on a project which merges two priority systems familiar to us here in the U.S. These are the structure-activity-relationship "Decision Tree" approach developed by the flavor industry, and the structure-category system based on FDA's own system for the priority-based assessment of food additives. Efforts at incorporating the concept of Consumption Ratio into the merged system are now underway.

The U.S. delegation will present a scientific proposal on the use of this combined priority-setting system at the next meeting of the Codex Committee on Food Additives in March 1987. The goal of this presentation is to demonstrate how priority-setting schemes can be combined to obtain an international approach to setting priorities for safety reviews. Activities such as this one serve as a splendid example of how industry, government, and nations throughout the world can work in a spirit of cooperation to address problems of mutual concern.

Conclusion

In conclusion, I'd like to remind you again of our shared responsibility: safe products for the world's consumers. Fragrances and flavors bring that sparkle of creativity, aura of elegance and touch of artistry which add quality to products worldwide. Together, let us continue to make certain they also bring the security that comes with knowing they are safe.

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