

Review of Research Programs
Center for Food Safety and Applied Nutrition
U.S. Food and Drug Administration

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I. Introduction

The Food and Drug Administration (FDA), a part of the U.S. Department of Health and Human Services, is a scientific regulatory agency with responsibility for the safety of foods, cosmetics, drugs, biologics, medical devices and radiological products. To accomplish its mission, FDA is organized into five centers with an associated nationwide system of field laboratories. The FDA has several advisory committees, one of which is The Science Board. This Board has recommended that the Centers' of FDA be reviewed periodically by special committees composed of non-FDA personnel that are chosen for their ability to critically evaluate the efficiency and effectiveness of these Centers. The current committee, working under the auspices of the Science Board, was assigned the task of reviewing the research operations of The Center for Food Safety and Applied Nutrition (CFSAN or Center). This Center has the mission of promoting and protecting the health and related economic interests of consumers by ensuring that the food supply is safe, nutritious, wholesome and properly labeled; and that cosmetics are safe and properly labeled.

CFSAN's responsibilities encompass the safety of all food except meat, poultry and egg products (CFSAN has responsibility for shells) which fall under the authority of the U.S. Department of Agriculture, and the labeling of alcoholic beverages and tobacco, which is regulated by the U.S. Department of the Treasury.

Membership of the CFSAN Review Committee (CRC) is listed in Appendix A.

The CRC was provided with informational materials prepared by CFSAN personnel approximately two weeks before the date of the review. The review began on the evening of April 13 with introductory remarks by Drs. Joseph Levitt, Bernard Schwetz, Alan Rulis and Robert Buchanan of CFSAN, and Owen Fennema, Chair of the Review Committee. During this session, the purpose of the review and the specific charge to the Review Committee were presented (Appendix B). On April 14 and 15, oral presentations were made by representatives of the six research groups in CFSAN (Regulatory Testing, Analysis and Color Certification; Methods Development; Antimicrobial Resistance and Tolerance; Prevention and Intervention

Program; Hazard Assessment, Applied Nutrition; Foods and Food Labeling) and each presentation was followed by a lengthy period of questions and answers. CFSAN presenters and accompanying panel members (Appendix C) did an excellent job of describing, with superb visual aids, the work currently being conducted. However, during the course of these presentations, the CRC had some difficulty in obtaining information about perceived problems and possible corrective actions, and, in some instances, about how essential the work being conducted was to fulfillment of the CFSAN mission.

The CRC deliberated in isolation on the evening of April 15 and the morning of the April 16.

II. CFSAN: Overall Evaluation

A. Quality

In general, the quality of CFSAN research programs was judged quite good however, the CRC noted considerable differences in quality among some of the six research groups. The weakest programs, because of insufficient numbers of scientists, appeared to be toxicology and applied nutrition, both of which are important components of CFSAN (see recommendation in "Balance" section).

B. Appropriateness

All of the major research programs reviewed was considered appropriate activities for CFSAN. The CRC believes research activities, of the types and level now being conducted, are barely adequate to support CFSAN's mission. Regulatory decisions by CFSAN must have a strong scientific basis if these decisions are to be respected by the courts, the public, those being regulated, and by countries that the U.S. is dealing with in international trade. It should be noted that many single food corporations have research groups larger than that of CFSAN, thus creating an obvious dilemma for CFSAN in its attempt to monitor and regulate the commercial food sector in a manner that is responsive, effective, and efficient.

RECOMMENDATION: CFSAN must maintain mission-related research programs of world class quality and of a size commensurate with obligations to fulfill its mission.

C. Balance

The President's Food Safety Initiative (FSI), commenced with resources insufficient to carry out the programs mandated, has created a funding imbalance for the six CFSAN research programs. The mandated emphasis on microbiological hazards, which is justifiable but inadequately funded, has resulted in the internal transfer of resources and personnel that has been especially harmful to the toxicology and applied nutrition programs. A few years ago, CFSAN was an acknowledged world leader in food toxicology, but this is no longer true. It is important that CFSAN reestablish its position of excellence in this area, because CFSAN cannot obtain all of the needed toxicological expertise from other governmental agencies.

RECOMMENDATION: CFSAN programs in toxicology and applied nutrition should be strengthened.

D. Personnel

A high quality scientific workforce is an essential component of a strong research program, and developing and retaining this kind of workforce is a major challenge for CFSAN. Furthermore, it is important that scientists be involved in the planning process, especially with respect to experimental approaches, and that they adapt to many changes as new research priorities and goals are formulated to meet the President's FSI. Some scientists are able to engage effectively in planning, and to adapt readily to change, but others are not. Adapting to new circumstances at CFSAN is especially difficult because scientists are often required not only to change their scientific discipline, e.g., chemistry to microbiology, but also to develop skills to write regulations associated with the new discipline. The expectation that scientists perform the dual tasks of research and formulation of regulations is considered by the Center as a sound approach to fulfilling its obligations, and the CRC agrees.

However, this approach does complicate the task of redirecting scientists to new fields of endeavor, especially when few support staff are provided (less than one per scientist) and training programs are insufficient.

CFSAN has successfully hired high quality scientists, and in certain areas, e.g., antimicrobial resistance and tolerance, has been able to retain them. Based on the number of peer-reviewed publications in respected journals, research productivity in CFSAN appears to be reasonable. However, the CRC believes that personnel management practices need improvement in several areas. The Center's program for professional development is undesirably weak; procedures used to evaluate employee performance are less than adequate; job descriptions apparently need improvement with respect to clarity and detail; and personnel classification at the GS11-15 levels appears to need evaluation for accuracy. The latter two aspects are expressed with qualification because the CRC was provided with only limited Information about these matters. Nonetheless, the point of overriding importance is that management of personnel must be done in accord with best practices otherwise employee morale, effectiveness and retention rates will suffer.

RECOMMENDATION:

- 1) Postdoctoral and student intern programs are needed to expose researchers and management to new views and to provide the Center with an effective means for evaluating potential new hires.
- 2) Increasing the number of support personnel per scientist should be a high priority objective of management. The present number of support staff is woefully inadequate and not cost effective. The consequences are inefficient research and decreased employee morale.
- 3) Procedures for reviewing the performance of research personnel need to be carefully evaluated and redesigned. These reviews should occur on a regularly scheduled basis and should focus on matters of research productivity, quality, impact relevance to the CFSAN mission, and ability of the researcher to interact effectively with associates. These reviews, if properly conducted, can be a powerful tool for improving employee morale and effectiveness. This matter should be a high priority consideration by CFSAN management.
- 4) The program for professional development should be greatly improved and expanded. This includes assuring that scientists regularly attend internal and external short courses in their areas of responsibility, attend at least one national or international scientific conference per year, have access to a sabbatical program, and are encouraged to accept

adjunct faculty positions at universities. The successful adoption of these initiatives should strengthen CFSAN's research programs, improve employee morale, and improve the Center's ability to develop reasonable, effective regulations and to respond rapidly and effectively to public health emergencies.

E. Management

The CRC recognizes that management practices are in a state of transition, and that improvements are being instituted. The need for improvement is evident to the CRC, especially in the areas of strategic planning, priority setting, implementation and accountability. How priorities are currently established was not explained in detail, thus, the CRC was inadequately informed to provide detailed advice on this matter.

However, it is very important that priorities be established annually by a process that involves pertinent input from all scientific personnel. Once established, an effective means should be devised to assess whether these priorities are implemented properly during the following year. The priorities should also be well publicized both in and outside the Center.

It was stated that a top-down system of management was being imposed however; its implementation was not evident, especially in terms of conformance of various research projects to stated priorities. (Note: Following the review, the CRC Chair was informed that the "top-down" system had been initiated for microbiology research in 1998, but had not yet been initiated for programs in chemistry, toxicology and nutrition). These matters are of great importance and improvements are needed. Part of the problem appears to lie with the inexperience and ineffectiveness of some of the middle managers. Suitable training and/or the hiring of new personnel for these positions should be considered.

The CRC recognizes that the current Director of CFSAN has been in office for a relatively short time, and to his credit, has made good progress in important staff appointments and in changing management practices of the Center. The current review occurred before the CFSAN administration had fully formulated its management plan and before much progress had been made in its implementation.

Consequently, the CRC's comments regarding administration of the Center's research activities must be considered in the context of the current state of change.

Based on statements made during the course of the review, it is clear that the Center is proud of its ability to respond quickly and effectively to emergency events, and the CRC believes that pride in this program is justified. CFSAN management appears to regard the research program of the Center as a major tool for attracting and retaining talented scientists for times of crisis. Whereas this is a valid use of the research program, care should be exercised to assure that the full range of CFSAN goals receive primary attention when establishing research priorities. In the current climate of increasingly limited resources and crises that occur frequently, this approach to research is imperative.

The CRC believes the Center Director recognizes most of these problems and is taking remedial action. It is important, however, that ensuing changes be based on a comprehensive strategic plan for CFSAN- one with a clear mission statement, clear objectives, conversion from a "bottom up" to "top down" management system (as is already being imposed), and defined measures of success, i.e., accountability. The strategic plan must be accompanied by carefully devised implementation procedures.

If a strategic plan had been available, CRC's evaluations of the appropriateness of various research activities would have been more detailed and reliable.

RECOMMENDATION: The CRC encourages the Center to move with dispatch to develop a strategic plan that provides clarity of mission and goals, and needed measures of accountability. Use of outside expertise to facilitate development and execution of the plan is advised. The plan must be devised so as to assure that:

- 1) CFSAN's regulatory programs are based on sound science and a risk assessment approach.

- 2) Management procedures are clearly stated and provide for accountability and

3) Determination of the appropriateness of various research activities can be easily determined.

This strategic plan will benefit the Center in several ways. Most importantly, it will provide clear guidance for organization, management decisions and operational practices. Publicizing such a plan will also enhance the Center's credibility, particularly if progress in attaining the stated goals is evident. Additionally, this plan will, if developed with participation of the CFSAN staff, serve as the "blueprint" for the culture change the Center must bring about.

RECOMMENDATION:

- 1) All personnel should be fully cognizant of the goals of their program. Each project should undergo a formal review annually and be evaluated for progress, current priority status, and likelihood that continuation will lead to success.
- 2) CFSAN should strive to move from its current FTE-based budgeting practice to one that is program based. Without such a change, true costs, effectiveness and accountability of research programs cannot be meaningfully assessed.
- 3) The Science Board and the FDA Chief Scientist should consider the present review as step 1 of a 3-step process. The second step should be a review of progress in developing CFSAN's management/strategic plan and should take place in 6-9 months. Only a few skilled reviewers are needed. Step three should focus on how well CFSAN research activities correspond to provisions of the strategic plan and should occur in about 12-18 months.

F. Other Matters

Appropriateness of Research Activities in Field Laboratories

Food safety research within FDA is being conducted at both CFSAN and the Office of Regulatory Affairs'(ORA) field laboratories. The CRC has concerns about duplication of effort, significance of impact, and usefulness of research results obtained at field laboratories. A few field laboratories appear to have convincing justification for conducting research, and have appropriate personnel, instrumentation and resources to accomplish their research objectives. The ones of concern to the CRC are those that do not have a compelling need to conduct

research, and do not have the personnel and resources to do so effectively. One or two persons spending 10% of their time on research cannot be expected to function in an effective manner. Basic studies in areas such as methods development and hazard assessment are clearly inappropriate for investigation at field laboratories, whereas studies on local problems or highly specific methodologies may be appropriate.

When research at a field laboratory is considered appropriate, care should be taken to assure that appropriate quality standards are maintained and that close collaboration occurs between researchers at the field laboratory and those at CFSAN. Collaboration of researchers at field laboratories with faculty members of local universities should also be encouraged to strengthen approved projects. Field laboratory personnel should be consulted when priorities for CFSAN research programs are established, and, similarly, CFSAN personnel should be closely involved in establishing priorities for research projects at field laboratories. (Note: following the review, the Chair of the CRC received information indicating that authorization for methods development in field laboratories, involves preparation of a proposal by the field analyst working in cooperation with a CFSAN scientist, and review of the proposal by a panel of CFSAN scientists using quality, relevancy and avoidance of redundancy as criteria). This supplementary information is appreciated, but the CRC stands by its previous comments and makes the following recommendation.

RECOMMENDATION: CFSAN should carefully review research programs at field laboratories and deactivate those programs that are too feeble to be effective, or are improperly focused. Cost savings that accrue from a paring of these activities should be used to augment research programs in well-established CFSAN laboratories.

Emergency Response Procedures

Although the CRC did not have an opportunity to evaluate in detail CFSAN's emergency response procedures, the Committee was left with a favorable impression regarding the effectiveness of these procedures. The only concern is that an emergency in one area will disrupt unduly the work of other programs as; personnel are assembled in response to the emergency.

The CRC believes that proper anticipatory planning would help minimize disruption of ancillary programs during these occasions.

Instrumentation

The CRC did not have an adequate opportunity to thoroughly evaluate the appropriateness of CFSAN instrumentation. However, our impression is that instruments (kinds, quality and amount) are, in general, adequate for fulfilling the CFSAN mission, but that many are not state-of-the-art.

RECOMMENDATION: CFSAN should prioritize its instrument purchases with great care.

Laboratory Certification

It is important that research results by CFSAN be acknowledged world wide as indisputable. Laboratory certification is an important prerequisite for attainment of this status.

RECOMMENDATION: CFSAN's laboratories should be certified.

Cosmetic Research

Research on cosmetics is an orphan program within FDA that historically has been located in CFSAN due to the presence of the food color/toxicology program. There appears to be no obvious disadvantage to having this program within CFSAN and some advantage to CFSAN arises from the presence of the associated instruments and personnel. It is important that FDA have competency in this area especially since the use of new bioactive substances (e.g., alpha hydroxy acids) in cosmetics has increased. Care should be taken to assure that activities in this area are well coordinated with similar activities in other groups outside CFSAN.

RECOMMENDATION: Activities in cosmetic research should be closely coordinated with other dermatology/transdermal research programs being conducted within FDA.

Codex Activities

RECOMMENDATION: Participation of CFSAN personnel in CODEX programs and other similar international programs is essential and should be continued.

Technology Transfer

Prompt and effective technology transfer is an important measure of CFSAN success. However, technology transfer activities are limited within CFSAN, and they relate primarily to assisting small companies and state health agencies in adopting Good Agricultural Practices and Good Manufacturing Practices.

RECOMMENDATION: CFSAN should, if they are not already doing so, develop tools to measure the effectiveness of the technology transfer process, and apply these tools on a routine basis.

III. CFSAN Evaluation: Individual Research Programs

A. Antimicrobial Resistance and Tolerance

Introduction

In the materials provided to the CRC, this program is said to focus on determining how pathogenic microorganisms adapt to natural and human-induced barriers to their growth. The purpose is to understand the adaptation mechanisms so that new control measures and regulations can be adopted as needed. Areas of special interest are the mechanisms by which pathogens develop resistance to antibiotics and resistance to control measures that are traditionally used by the food industry, such as alteration of pH or water activity, heating, and the use of chemicals.

Evaluation and Recommendations

The term "Antimicrobial Resistance and Tolerance" does not clearly describe the activities of this group and leads to misconceptions and possibly unfulfilled expectations. The main and most visible activities relate to the emergence of virulent lineages of food borne pathogens and the underlying molecular genetic mechanisms.

Because the title and activities do not match well, some expectations appear to be left unfulfilled, despite the research being of excellent quality. The fault lies more with management and vision than it does with the quality or intrinsic relevance of the research. The development and epidemiology of antimicrobial resistance, including resistance to commercial disinfectants and processing intervention procedures, and the emergence of antibiotic resistant organisms as they relate to food manufacturing and processing practices, are highly relevant to CFSAN's mission, but are not strengths of this program. The topic of emergence of antibiotic resistant organisms is being addressed by the FDA Center for Veterinary Medicine (CMV), and CFSAN's work in this area should be carefully coordinated with that of the CMV.

RECOMMENDATION: Change title of this program to: "Emergence of virulence and antimicrobial resistance among food borne pathogens." This will more clearly associate activities of this program to the Center's mission, and will provide guidance for future program development.

The research on pathogen emergence is excellent and clearly makes an important contribution to establishing the credibility of research at CFSAN. This is a fine example of the type of world-leading research that CFSAN must produce if it is to maintain its position as a "center of excellence." This expertise was of central importance in national deliberations on the use of antibiotic resistance determinants in agricultural genetic engineering because it enabled CFSAN to serve as a respected neutral consultant and provide valuable advice to companies seeking guidance in this area. Such illustrations of the practical benefits that can arise from basic research, and the relevance of this type of technology transfer to CFSAN's regulatory mission, were not highlighted in the review process. This, and other similar examples, should have been used to demonstrate that relevant research is a critical prerequisite for fulfillment of CFSAN's mission.

RECOMMENDATION: Priorities for work in the area of Antimicrobial Resistance and Tolerance should be clearly established.

Because of the FSI and other initiatives, research on the emergence and physiology of food borne pathogens, particularly with reference to resistance to processing procedures and various agents, is of increased relevance to CFSAN's mission. The emergence of antibiotic resistant food borne pathogens and the role of food in their dissemination is an important area that deserves attention. Center scientists are uniquely positioned to explore these matters. It is not clear, however, that all current projects relate well to these topics. For instance, developing detection methods for the polymerase chain reaction in food borne pathogens might fit more appropriately under the aegis of the Methods Development group. In addition, it was unclear whether this line of research was essential to the successful accomplishment of the CFSAN mission, was a state-of-the-art orphan project, or was simply of commercial interest. In contrast, studies on the mechanisms of emergence of food borne pathogens are well conceived and important.

RECOMMENDATION: Research on antibiotic resistance of microorganisms is of major importance and should be carefully integrated in a cross-center effort. This subject is also of

central importance to the Center for Veterinary Medicine and other centers.

The CRC is not convinced that all aspects of the work on induction of acid tolerance and DT 104 are unique. Work of this kind is being conducted in universities and other federal agencies and the degree of collaboration is not clear. This work should be carefully coordinated with current research at universities. Results from this research are relevant to new processes being developed by the food industry and should be considered when standards for these processes are developed. Information provided to the CRC regarding CFSAN research on *Ustera* epidemiology and *Salmonella*, was insufficient to enable the uniqueness and quality of this work to be judged.

Other areas that are pertinent to the activities of this group are the relationship between biofilm physiology and resistance of microorganisms to disinfection procedures, and food as a vehicle for the transmission of antibiotic resistant organisms.

RECOMMENDATION: The CRC is supportive of most of the research being conducted in this area, and the presence in CFSAN of persons with the skills needed to conduct this research. This group has an important role in emergencies involving food pathogens. It is imperative that the research conducted be of the highest quality so that results generated will be accepted as valid by all parties when crisis events arise.

B. Hazard Assessment

Introduction

The hazard assessment program comprises two areas of focus: chemical toxicology and microbial risk analysis. The stated goal of the programs is to identify the scope of hazardous effects of chemical and microbial toxicants and to define their dose response relationships under various regimens of exposure.

Evaluation and Recommendations: Chemical Toxicology

The hazard assessment program for chemicals serves primarily as support for other CFSAN programs rather than as a stand-alone research effort. The program appears to have a

conventional toxicology screening focus. There are few examples of cutting-edge research in this area, although the dermal assessment program is well respected and unique. While CFSAN has a proud history of toxicology excellence, it has lost its leadership role in this field. The program's efforts are currently misdirected and are not consistent with modern toxicological practices, i.e., they do not have a risk-based focus. The program -does not deal with chemical mixtures or food-related biotechnology issues, and its role in FDA's regulatory mission is unclear.

For example, it does not appear to be linked to the nutritional programs of CFSAN, a relationship that would strengthen both programs.

FDA needs a strong chemical toxicology program to support CFSAN's mission and regulatory activities. There is no other regulatory toxicology program that tests cosmetic components and food additives.

RECOMMENDATION: Management should determine which aspects of research in chemical toxicology should be in CFSAN and which aspects can be provided by other governmental groups. Those aspects that support CFSAN's unique regulatory responsibilities should be strengthened in-house as well as through partnerships with other organizations. For example, CFSAN should consider partnering with, and in some cases depending on, state-of-the-art toxicology laboratories, such as FDA's National Center for Toxicological Research.

Evaluation and Recommendations: Microbial risk

Microbial risk assessment is a small but rapidly developing field. This is a new program for FDA, established primarily in response to the FSI. World-class experts in microbial risk assessment have been hired, and collaborations with the Joint Institute for Food Safety and Applied Nutrition (JIFSAN) and the Risk Assessment Consortium have been developed. These initiatives provide an opportunity for CFSAN to develop national and international leadership in this area. However, resources are sufficient for only two quantitative risk assessments (e.g., Listeria and Vibrio) annually. For a center whose activities are devoted overwhelmingly to the public health impact of microbial contaminants in food, and which purports to be moving toward a risk-based regulatory framework, the inability to conduct more than two microbial risk assessments annually is a serious shortcoming.

An outstanding program in microbial risk assessment is essential if FDA is to fulfill its regulatory mission in a satisfactory manner. The current program is unique and has the potential to develop an important new area of risk assessment in which FDA must assume a leadership role. This program will, if properly developed, become a signature program of CFSAN and greatly enhance the Center's credibility and effectiveness.

RECOMMENDATION: CFSAN's microbial risk assessment program should be helping to establish improved HACCP protocols. CFSAN's in-house capability in microbial risk assessment should be enhanced with additional personnel and resources to help propel CFSAN toward a leadership role in this field. Partnering with other world experts, in the US and other countries, should be considered to facilitate development of common methodologies and enable broader coverage. In addition to developing methodologies, a greater number of risk assessments should be performed annually to facilitate control of microbiological hazards. Methodologies for determining "acceptable" levels of risk for use in regulating microbial contaminants are also needed. Current partnerships with the Center for Disease Control (CDC) and use of international data bases should continue to be emphasized, as should evaluation of risks from microbial contaminants in actual food matrices.

Evaluation and Recommendations: Balance Between and Common goals for the Programs in Chemical Toxicology and Microbial Risk

Because of the FSI, CFSAN research has undergone a pronounced shift away from chemical toxicology to pathogenic microorganisms. The CRC believes this shift has been excessive and the toxicology program has suffered unduly. For example, food allergies and sensitivities are important areas for CFSAN, yet these areas are receiving little attention. To best assure public health protection, a public health-based process for setting priorities in chemical and microbial toxicology is needed. This process should be a top-down approach starting with evaluation of public health problems and then identification of potential causes of the problems as a guide to solving them. Research and regulatory priorities based on a public health approach will help assure that limited resources are used most effectively. While responding to emergencies is an important role that CFSAN does well, a comprehensive priority setting process based on evaluation of key public health issues would position CFSAN proactively as well as reactively. CFSAN's recent priority-setting exercise and JIFSAN's activities are good steps in this direction.

RECOMMENDATION: To use risk assessment appropriately in regulation, CFSAN should develop a public health-oriented approach to establish regulatory priorities for hazardous chemical and microbial agents. The priorities established should encompass the full food chain from pre-harvest to consumer. Because CFSAN alone does not have the mandate or resources to conduct a comprehensive assessment of public health, it should collaborate with other agencies.

C. Methods Development

Introduction

Analytical methods, properly developed and validated as suitable for the intended purpose, must be used to generate data of the quality needed to support CFSAN's regulatory rulemaking and enforcement actions, as well as for defending its actions in courts of law. Development of analytical methods consumes a major portion of the time of the CFSAN research staff, and the results benefit nearly all offices within the Center.

More specifically, development of methods to detect and quantify microbiological agents, toxicants and essential nutrients is critically important to the regulatory mission of FDA. The emergence of new pathogens and toxins accentuates the importance of this type of research. The more rapidly the procedure can be performed, the more useful it is likely to be for assuring and regulating the safety of the food supply. Approximately one-third of Center's research budget is committed to methods development and the CRC believes this is appropriate.

Evaluation and Recommendations

CFSAN scientists are among the leaders of the world in developing methods for detecting potentially hazardous agents in foods, and its research is innovative and appropriate. The committee commends researchers in this group for the high quality of their research 'accomplishments. However, some redirection of this group's priorities may allow limited resources to be used more effectively. For example, some CFSAN projects deal with the development of rapid methods, particularly for the detection of pathogens (e.g. E. coli 0157:H7) in foods. This work appears to overlap with research being conducted by private companies, academia, and other governmental agencies.

An adequate strategic approach to prioritizing work on methods development does not appear to exist within CFSAN and this situation needs to be corrected.

RECOMMENDATION:

- 1) The FDA should develop an agency-wide plan for method development research. A strategic approach using defined criteria for priority setting should be adopted. This process should involve all relevant governmental centers both within and outside the FDA. All aspects of food safety should be addressed. A strategy should also be developed to prioritize the development of methods for detecting new agents of public health concern. Direct ties to overall program priorities and research plans should be in place.
- 2) CFSAN should carefully monitor the activities of the private sector, other governmental agencies, and academia in developing rapid methods for specific pathogens, toxins and chemicals and enter into collaborative arrangements when these are feasible and effective. Management should also identify and prioritize the individual microorganism

or toxin for which rapid methods are most needed and communicate these priorities to potential developers in the private sector to help avoid duplication of effort.

D. Prevention and Intervention Program

Introduction

CFSAN provides guidance on the acceptability of various techniques used by the food industry for avoidance of food borne diseases. Strategies for the production of high quality agricultural commodities that are less likely to support pathogen survival and growth are included in the scope of its activities. Outcomes from these activities are science-based policies/regulations that are valuable for developing and monitoring inspection and Hazard Analysis Critical Control Point (HACCP) programs.

Some examples of projects included in CFSAN's Prevention and Intervention program are: (1) development of procedures to improve the safety of sprouts, apple cider, and seafood, (2) determination of pathogen survival during 60-day aging of hard cheese products made from fresh milk, (3) evaluation of the suitability of new packaging materials for irradiated prepackaged foods, and (4) validation of the microbial safety of new non-thermal processes and extended shelf-life foods.

Evaluation and Recommendations

Without the information provided by the kinds of projects cited in the introduction, CFSAN would be unable to properly evaluate the safety of new technologies and to formulate sound, science-based regulations governing how these technologies are employed.

RECOMMENDATION: The CRC endorses CFSAN's research activities to determine safe practices for new or modified food processes, but recommends that management regularly: (a) evaluate these projects for conformance to CFSAN priorities, progress and impact, and (b) determine for each project how the objectives can be achieved most effectively and efficiently, i.e., should the studies be conducted in-house, in collaboration with other groups, or by contract with other parties?

To attain the goals of the Prevention and Intervention program, research collaboration is underway among CFSAN-Washington, DC, CFSAN-Dauphin Island, The National Center for Food Safety Technology (NCFSTI Moffett Center), USDA Agricultural Research Service, University of Illinois, University of California at Davis, University of Maryland, the State of California, Durango County, California, and the food industry.

These collaborative ventures appear to be working well. For example, the CFSAN/National Center for Food Safety Technology partnership in Illinois is an excellent example of how various groups with interests in food safety regulation can work together effectively.

RECOMMENDATION: The CRC endorses research collaboration among various groups with interests in food safety practices and regulations, provided these collaborations have been determined to be the most effective and efficient approaches available. Factors that should be considered when contemplating collaboration include: availability of appropriate personnel, equipment and facilities; cost effectiveness of various alternative options, and likely long-term effectiveness of the partnership.

Globalization of food production and distribution is occurring rapidly and this raises broad new challenges for CFSAN. An important concern is the safety of food, especially fresh fruits and vegetables, being imported into the U.S.

RECOMMENDATION: CFSAN should be a world leader in establishing standards and procedures (reliable sampling procedures; rapid, accurate and economical tests) for assuring the safety of foods crossing international boundaries. Safety when leaving the country of origin should be emphasized.

E. Regulatory Testing, Analysis and Color Certification

Introduction

Regulatory testing/analysis activities focus on the collection and analysis of samples to determine compliance with existing regulations. Collected data are used to initiate enforcement actions and to support the Center's position in potential challenges by the regulated industry.

Research in the color certification area is conducted to provide CFSAN with relevant information for future regulatory actions, to improve test methods and to provide testing guidance to industry. This is a unique, service-oriented program with industry as the client. The program operates on user fees and is self-sustaining

Evaluation and Recommendations: Color Certification Program

Retaining the color certification program within FDA provides credibility to the certificates that are issued because of the exacting standards imposed by FDA. Another benefit of this activity is that it provides skilled professionals and instruments that are useful to other programs within CFSAN.

RECOMMENDATION: Relative to the research component of the Color Certification Program, new methodologies and instrumentation should continue to be evaluated and introduced to enhance the quality of service to clients and to maintain state-of-the-art skills within CFSAN.

Evaluation and Recommendations: Regulatory Testing

This activity consists of sampling and sample analyses for problem identification and emergency response. The focus is on potential major outbreaks of food borne illness, adulteration, and other risks to public health. This activity appears to be outbreak oriented and does not address the possibility of widely scattered isolated cases, other than through PulseNet. The goal is to limit adverse effects on public health through early identification of unsafe food, and conditions that can lead to unsafe food.

Regulatory testing within CFSAN is a highly visible, mandatory function which must continue to operate efficiently and with the highest standards of excellence if CFSAN's mission is to be successfully accomplished. Fifteen percent of the Center's resources are devoted to this activity. As threats to public health arise, CFSAN must quickly assess the seriousness of the event, and determine the means, magnitude and duration of response. Uncertainties associated with

emergencies complicate the process of achieving timely responses that are effective and efficient, and these emergencies are often disruptive to other programs in the Center. The CRC believes that current procedures for emergency response are very good in terms of speed and scientific quality. Attainment of highly credible results requires that emergency response procedures be conducted in accord with the highest standards of laboratory practice.

RECOMMENDATION:

- 1) The Center needs to carefully devise management procedures for emergency events so that these events will not disrupt other activities. Although emergency events cannot be eliminated, management should attempt to develop systems and regulations that lessen their frequency and seriousness.
- 2) CFSAN laboratory practices should conform to the principles of the AOAC Food Laboratory Accreditation Working Group (FLAWG). Consideration should also be given to achieving full ISO 25 accreditation for CFSAN laboratories.

F. Applied Nutrition, Foods and Food Labeling

Introduction

This program is unique within CFSAN because it does not relate to food safety; it has diverse responsibilities, and the types of investigations conducted differ greatly from those of other CFSAN groups. Rather than basic biomedical research in the conventional sense, the work of this group is applied in nature. It involves conducting surveys and other forms of data collection and data analysis, with a focus on human behavior, disease prevention, and formulation of policies. During the past decade, several Acts of Congress (e.g., the Nutritional Labeling and Education Act, and the Dietary Supplement Health and Education Act) have created a climate of greatly increased demand for research in applied nutrition. This is especially evident in research to support mandated FDA regulatory activities in food labeling, fortification, and dietary supplements. These external demands determine the focus of program activities, thereby precluding development by CFSAN of a long-term research agenda based on evaluation of public health risk. The group's excellent and extensive work on folate fortification, a project that

originated because of external mandates, provides a good example of why this group needs to exist within CFSAN and what level of funding is needed to allow it to function effectively.

Evaluation and Recommendations

The applied research on fortification policy and consumer understanding of food labels is unique, strong, and useful. Analytical research on nutritional and natural products is adequate, and the research on infant formulas and medical foods is modest, but also adequate.

Without a strategic plan in place for research in applied nutrition, it is difficult to accurately assess its appropriateness to the CFSAN mission. The research presented appears to be justifiable because it is closely linked to the Center's regulatory responsibilities.

The Committee is concerned that the intense demands for research on crisis issues will interfere with research conducted in anticipation of future needs. This program is on the verge of becoming overwhelmed by concerns and opportunities that arise about various conventional nutrients and dietary supplements. If this occurs, adequate attention to emerging topics such as nutraceuticals and functional foods will not be possible.

RECOMMENDATION:

- 1) A long-term strategic plan for dealing with critical issues related to food and nutrition should be developed. This plan should be based on public health needs as revealed by the National Nutrition Monitoring Programs.
- 2) Research should not duplicate that which is being conducted elsewhere, and partners should be sought whenever appropriate and possible. For example, the CRC noted that research on soy products and their effects is currently underway at Iowa State University, University of Illinois, Loma Linda University and other institutions. Thus, work at these institutions should not be duplicated by CFSAN.
- 3) The Committee recommends that this program continue to seek collaborative arrangements with USDA-ARS for expertise in natural products and in food composition.

Because little is known about the properties of many herbal and botanical dietary supplements now on the market, and there are 1,500-1,800 such products, the research demands in this area will surely exceed the Center's current capabilities.

RECOMMENDATION: CFSAN should promote a JIFSAN-led Interagency Task Force on “Supplements, Natural Products, Nutraceuticals and Functional foods” to develop research partnerships with other universities and agencies. Similar strategies could be used to expand applied nutrition research in areas such as food allergens, which will require increasing attention from a regulatory standpoint.

IV. Critique of the Review Procedure

Although the CRC believes the results of this review will be of considerable value to CFSAN management, much greater value would have been achieved if preparations by CFSAN personnel had been more complete and appropriate. Reviews of the greatest value begin with a careful process of self-evaluation by the party being reviewed. If results of the self-evaluation-perceived problems, concerns and suggestions for change-are provided to the review committee well in advance of the on-site review, then the value of discussions during the review will be greatly enhanced. CFSAN did not provide the CRC with self-evaluation information and this impaired the CRC's ability to make insightful recommendations in some areas and precluded recommendations in others. The CRC sincerely believes that failure of CFSAN to provide the CRC with the results of a self-evaluation occurred because of inexperience with a well-designed review process and because detailed instructions were not provided.

It also would have been of great help to the CRC if CFSAN management had, at the outset, clearly and concisely identified its mission, specific objectives, successes and failures, and its role in FDA's mission.

By assuming, improperly, that CFSAN management was familiar with the desired review protocol, the CRC Chair must accept some blame for these deficiencies in the review process. The Chair did not discover these problems until about 10 days before the review, at which time rectification was difficult.

RECOMMENDATION:

- 1) The FDA Science Board should prepare guidelines on “How to Prepare for a Review,” and these guidelines should be provided to the group that is scheduled for review at least six months in advance for the review.
- 2) Additional reviews of FDA programs should not be conducted until these guidelines are available.

Date: July 1, 1999

Owen Fennema

On behalf of the Review Committee

APPENDIX 1

SCIENCE BOARD SUBCOMMITTEE

Chair:

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APPENDIX 2

OBJECTIVES OF THE CFSAN REVIEW

To improve the operating procedures and management practices of CFSAN so that it can:

- Continually and easily up-date its priorities in accord with needs
- Accomplish its mission-related tasks more rapidly, efficiently, and effectively.

REVIEW CHARACTERISTICS NEEDED TO ACCOMPLISH OBJECTIVES. The Review Committee must dedicate itself to careful, fair evaluation of the information presented, and adopt an attitude of constructive criticism. CFSAN presenters must be willing to fully explore program weaknesses, strengths, and problems, and offer thoughtful suggestions regarding changes that might be helpful. ..

APPENDIX 3

Presenters and Panel Members

Regulatory Testing and Analysis

Presenters:

George P. Hoskin, Ph.D. Director
Division of Science and Applied Technology
Office of Seafood, FDA

John E. Bailey, Ph.D.
Director Office of Cosmetics and Colors, FDA

Panelists:

Naomi Richfield Fratz, Ph.D.
Chief, Color Certification Branch
Division of Programs and Enforcement Policy
Office of Cosmetics and Colors, FDA

Robert Lee Bowers
Director, Division of Enforcement
Office of Field Programs

Joe Betz, Ph.D.
Acting Chief, Biological and Organic Chemistry Branch
Division of Natural Products
Office of Plant and Dairy Foods and Beverages

Farukh Kambaty, Ph.D.
Microbiologist Division of Microbiological Studies
Office of Special Research Skills

Antimicrobial Resistance and Tolerance

Presenters:

Barbara McCardell, Ph.D.
Acting Director, Division of Virulence Assessment
Office of Plant and Dairy Foods and Beverages

Thomas A. Cebula, Ph.D.
Director, Division of Molecular Biological Research and Evaluation
Office of Premarket Approval

Panelists:

Robert L. Buchanan, Ph.D.
Senior Science Advisor

Steven M. Gendel, Ph.D.
Chief, Biotechnology Studies Branch Division of Food Processing and Packaging
Office of Plant and Dairy Foods and Beverages

Methods Development

Presenters:

Steve Musser, Ph.D. Analytical Chemist Chief, Instrumentation and Biophysics Branch
Division of General Scientific Support
Office of Scientific Analysis and Support

Jan Johannessen, Ph.D.
Toxicologist Toxicological Effects Branch
Division of Toxicological Research
Office of Special Research Skills

Peter Feng, Ph.D.
Microbiologist Acting FSI Research and Risk Assessment Lead
Division of Microbiological Studies
Office of Special Research Skills

Panelists:

George J. Jackson, Ph.D.
Director, Office of Special Research Skills

Sam Page, Ph.D.
Scientific Director Joint Institute for Food Safety and Nutrition

Prevention and Intervention

Presenters:

Dave Annstrong, Ph.D.
Associate Director for Research
Office of Plant and Dairy Foods and Beverages!
National Center for Food Safety and Technology

Art Miller, Ph.D. Senior Scientist
Office of Special Research Skills

Panelists:

Karen Carson Acting Deputy Director
Office of Plant and Dairy Foods and Beverages

Patricia Hansen, Ph.D.
Regulatory Policy Branch Division of Product Policy
Office of Premarket Approval

R. Merrill McPhearson, Sc.D.

Gulf Coast Seafood Laboratory Branch Division of Science and Applied Technology

Office of Seafood

Hazard Assessment

Presenters:

Neil Sass, Ph.D.

Special Assistant to the Center Director Acting Director,

Division of Toxicological Research

Office of Special Research Skills

Richard Whiting, Ph.D.

Senior Scientist Special Assistant to the

Office Director Office of Plant and Dairy Foods and Beverages

Panelists:

Michael Bolger, Ph.D., DABT Chief, Contaminants Standards Monitoring and Programs

Division of Programs and Enforcement Policy

Office of Plant and Dairy Foods and Beverages

Robert Bronaugh, Ph.D.

Supervisory Toxicologist Cosmetic Toxicology Branch

Division of Science and Applied Technology

Office of Cosmetics and Colors

Michael Dinovi, Ph.D.

Special Assistant to the Division Director Division of Product Manufacture and Use

Office of Premarket Approval

John Kvenberg, Ph.D.

Acting Deputy Director Office of Field Programs