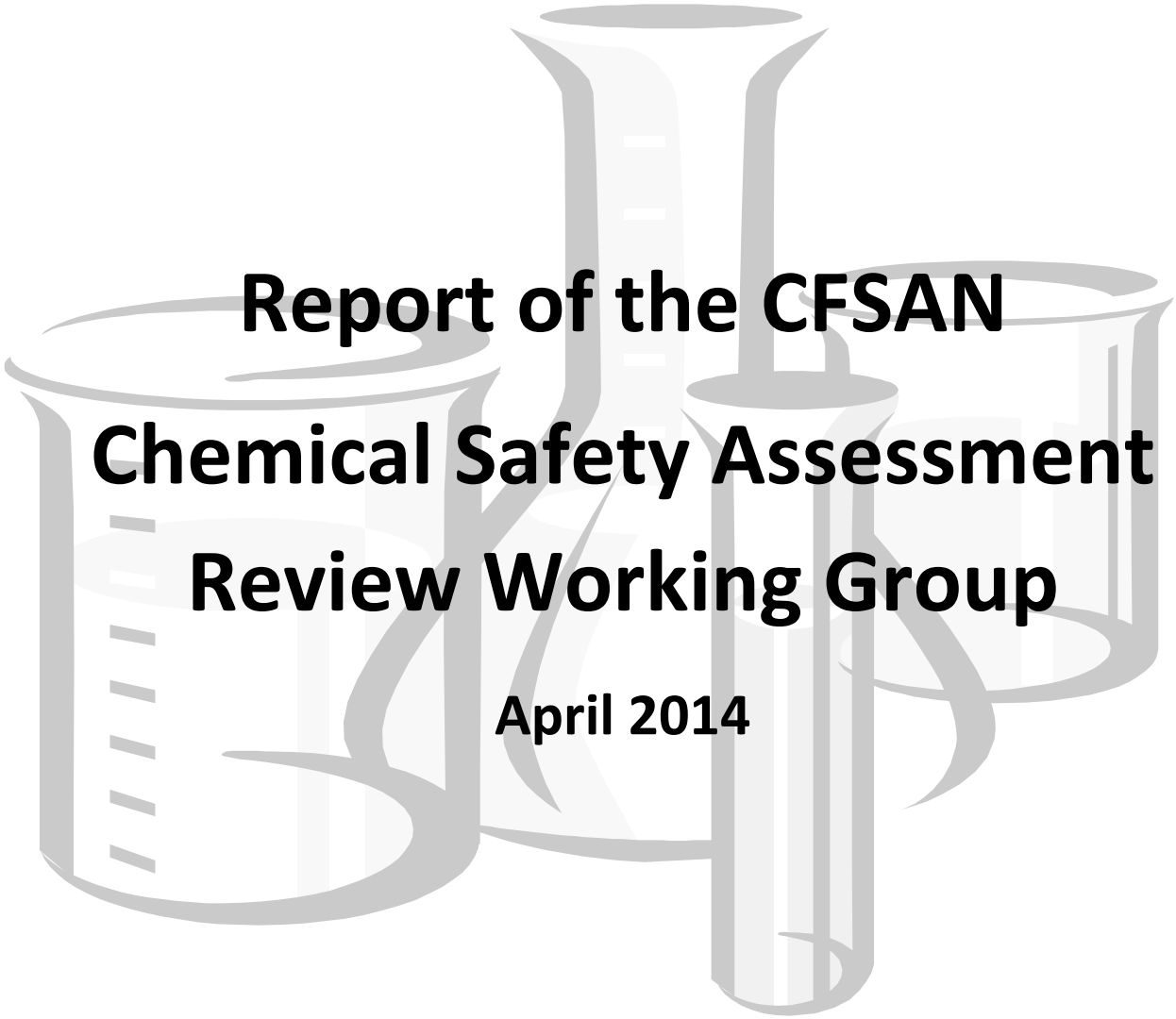
OFVM



Report of the CFSAN Chemical Safety Assessment Review Working Group

April 2014

REPORT OF THE CFSAN CHEMICAL SAFETY ASSESSMENT REVIEW WORKING GROUP

Evaluation and Summary of the Results of the FDA OFVM Program Review of CFSAN's Chemical Safety Program

EXECUTIVE SUMMARY

FDA's Office of Foods and Veterinary Medicine (OFVM), which encompasses both the Center for Food Safety and Applied Nutrition (CFSAN or the Center) and the Center for Veterinary Medicine (CVM), must make effective and efficient use of its chemical safety resources, act to ensure the rigor and effectiveness of its chemical safety program responsibilities, and maintain and work to strengthen its national and international leadership role to meet current and future challenges in the field of chemical safety. To help accomplish these goals, OFVM initiated a review of its overall chemical safety assessment program, focusing on the scientific capacity and management of the program's multiple elements across CFSAN and CVM. This review involved:

- Anonymous and confidential interviews of employees involved in all the elements of OFVM's chemical safety assessment program;
- Anonymous and confidential interviews of CFSAN alumni and senior managers from other Federal agencies experienced in chemical safety assessment; and
- Five listening sessions conducted by CFSAN with internal and external stakeholders on OFVM's overall chemical safety assessment program.

In addition, four outside consultants, all of whom are considered experts in the field, and who had previously held senior management positions dealing with chemical safety assessment in the Federal government, met with OFVM and senior CFSAN managers to discuss the interview and listening session reports. Based on this discussion and their review of the interview and listening session reports, each consultant also made his or her own written recommendations for OFVM's chemical safety program.

CFSAN's Center Director formed an internal Chemical Safety Working Group (the Working Group) to review all the reports and consultant recommendations, and directed the group to develop this report, which identifies the most significant issues arising from the various reports and contains prioritized recommendations for improving the chemical safety program at CFSAN, along with a plan to implement the recommendations.

The issues and recommendations offered in this report are in the context of chemical safety unless otherwise indicated and fall into three broad categories:

- Science;
- Communication and Collaboration; and
- Training and Expertise.

Science Recommendations

Principal recommendations in the science are as follows:

- Establish an *in silico* knowledgebase to assist in the proactive identification and ranking of emerging chemical hazards, risks, and new science. *In silico* refers to information obtained using a computer or via computer simulation, in contrast to information obtained from biological systems (*in vivo*, *in vitro*, and *in situ*).
- Increase the availability of and access to databases to improve the strength and reliability of hazard identifications and safety/risk assessments.
- Promote the development of mechanisms and forums that increase communication and exchange among toxicologists to improve and encourage scientific excellence, understanding, and consensus, and thus consistency in CFSAN's chemical safety/risk assessments.
- Increase opportunities for cross-organizational internal peer review of chemical safety projects.
- Increase engagement with other Federal agencies to leverage their scientific expertise as a resource on major chemical safety/risk assessments and other key work products.
- Determine to what extent consistency on the methodology used for chemical safety/risk assessment between and across offices at CFSAN and between CFSAN and CVM is achievable.
- Develop standard operating procedures (SOPs) to help ensure consistency within CFSAN Offices on chemical risk assessments/safety assessments.

Communication and Collaboration Recommendations

Principal recommendations in the communication and collaboration area are as follows:

- Institute more formalized and routine meetings among management and staff to share information on work-related projects, priorities, and regulatory decisions.
- Formalize procedures (SOPs) for initiating and managing collaborations between CFSAN Offices and with external organizations (e.g., academia, other Federal agencies, and Centers of Excellence).

- Explore where Memoranda of Understanding (MOU) or other mechanisms can be implemented to facilitate collaborations with other Federal agencies and international bodies.
- Create a mechanism that is widely used and frequently updated to identify both internal and external expertise, as a means to identify possible collaborators.
- Establish SOPs for research collaborations between CFSAN and the National Center for Toxicological Research and NTP and ensure that all researchers receive training on the SOPs.

Training and Expertise Recommendations

Principal recommendations in the training and expertise area are as follows:

- Develop better method(s)/tools for identifying, tracking, and engaging subject matter experts (SMEs) both within FDA/CFSAN and within other government organizations.
- Identify points of contact within Offices, Centers, and other Federal agencies to pursue collaboration on emerging issues.
- Increase the use of integrated teams and matrix management to address specific issues and special projects.
- Make training and continuing education on a regular basis a required part of individual performance plans.
- Develop focused programs to minimize gaps in scientific expertise caused by anticipated personnel changes (e.g., retirements and promotions), and unanticipated personnel changes (e.g., employee departures).
- To the extent possible, increase resource allocation for training and continuing education.
- Work with CFSAN Staff College to develop science training courses in chemical safety/risk assessment.
- Explore opportunities for providing training at other Center Staff Colleges (e.g., CDER, CDRH).
- Partner with various professional societies to bring training to CFSAN.

The Working Group was concerned that without a plan to go forward and to track implementation progress, many recommendations in this report might languish. Therefore, the concluding section of the report contains a suggested implementation plan that organizes the recommendations according to the time the Working Group thinks it will take to implement, rated as to whether it is short, medium, or long-term. (For purposes of this report short-term was defined as being able to initiate within 3-6 months; medium-term is within 6-18 months; and long-term is within 18 months-4 years.) The Working Group believes that implementation of the recommendations contained in this report will significantly improve the effective and efficient use of CFSAN's chemical safety resources, and help to ensure the rigor and effectiveness of the

chemical safety program and maintain and strengthen its national and international leadership role in food and cosmetic chemical safety.

INTRODUCTION

The FDA Office of Foods and Veterinary Medicine (OFVM) Program encompasses a wide range of responsibilities and activities of the Center for Food Safety and Applied Nutrition (CFSAN or Center), and the Center for Veterinary Medicine (CVM). Carrying out FDA's food safety and nutrition activities becomes more challenging every year as globalization, advances in science and technology, and shifts in consumer preferences and expectations drive change throughout the different aspects of the human food system.

Regulating the safety of chemicals in food and cosmetics – ranging from intentionally used additives and colors to unavoidable contaminants – is central to the public health mission of CFSAN. The Center has a long history of national and international leadership in chemical safety based on its substantial expertise and experience in toxicology, risk assessment and chemical safety regulation.

CFSAN's chemical safety program currently faces significant challenges due to new chemical technologies that are being developed and used in the processing or manufacture of food and cosmetics, along with new methods of identifying and assessing chemical hazards. The chemical safety program is also affected by resource constraints and public expectations, among other things.

OFVM must make effective and efficient use of its chemical safety resources, act to ensure the rigor and effectiveness of its program, and maintain and work to strengthen its national and international leadership role to meet today's challenges in the field of chemical safety. To help accomplish these goals, the leadership of OFVM initiated a review of its overall chemical safety assessment program, focusing on the scientific capacity and the management of the program's multiple elements across CFSAN and CVM.

The focus of this report is the evaluation of the findings of the OFVM program review with respect to the responsibilities and activities of CFSAN in the area of human food and cosmetic chemical safety. The goal of the review was to assess the capacity of CFSAN's current chemical safety assessment program, how that capacity is deployed and applied across the program, and how staff and resources are managed across the program's multiple elements in CFSAN and CVM. The OFVM review also examined the nature of the relationship and interactions between CFSAN and other U.S. government agencies, international organizations, the external scientific community, and other external stakeholders within the realm of its activities in the area of chemical safety. The review is intended to lead to improvements and enhancements in many areas so CFSAN (and CVM) can better meet today's chemical safety assessment challenges.

CFSAN's Programs in Chemical Food and Cosmetic Safety

Chemical safety assessments occur in four different operating units in CFSAN- the Office of Food Additive Safety (OFAS), the Office of Cosmetics and Colors (OCAC), the Division of Dietary Supplement Products (DDSP) in the Office of Nutrition, Labeling, and Dietary Supplements (ONLDS) and the Division of Risk Assessment (DRA) in the Office of Analytics and Outreach (OAO). In addition, research to support CFSAN's Chemical Safety Program is conducted in its Office of Applied Research and Safety Assessment (OARSA) and the Office of Regulatory Science (ORS) and on occasion at FDA's National Center for Toxicological Research (NCTR) and at the National Toxicology Program by the National Institute for Environmental Health. The chemical safety assessment and research work of these groups also serves to support the regulatory and compliance activities of other CFSAN offices such as the Office of Food Safety and the Office of Compliance.

Food Additives- OFAS has regulatory authority over direct and indirect food additives, and color additives. Direct food additives are those that are added to a food for a specific technical effect such as appearance, shelf life, or stability. Most direct additives are identified by name on the ingredient label of foods. Any substance the intended use of which results or may reasonably be expected to result, directly or indirectly, in becoming a component or otherwise affecting the characteristics of food is a food additive, and is subject to premarket review and approval by FDA, unless the substance is generally recognized, among qualified experts, as having been adequately shown to be safe under the conditions of its intended use (GRAS exemption), or unless the use of the substance is otherwise excluded from the definition of a food additive. Indirect food additives (the statutory term is food contact substances) are additives that become part of food as a result of direct contact. This may be due to packaging, storage or other handling. For instance, trace amounts of packaging substances may migrate into foods during storage.

A color additive is any dye, pigment, or substance which when added or applied to a food, drug or cosmetic, or to the human body, is capable (alone or through reactions with other substances) of imparting color. (A color additive for use in or on a device is subject to the color additive provisions only if it comes in direct contact with the body of man or other animals for a significant period of time.) FDA is responsible for ensuring that color additives are safe. There is no GRAS exemption for color additives.

In enacting the Food Additives Amendment of 1958 to the Federal Food, Drug, and Cosmetic Act of 1938, Congress acknowledged that absolute safety is not possible. Therefore, the law establishes, based on the best available science, a safety standard of a reasonable certainty of no harm for food additives, GRAS substances, and color additives under the intended conditions of use.

Dietary Supplements- CFSAN regulates both finished dietary supplements and dietary ingredients (e.g., herbs, vitamins). The manufacturer of a dietary supplement or dietary ingredient is responsible for ensuring that its supplement or ingredient is safe before it is placed on the market. If a manufacturer wishes to market a dietary supplement that contains a "new dietary ingredient (NDI)" and the NDI has not been present in the food supply as an article used for food in a form in which the food has not been chemically altered, the manufacturer must submit to FDA, at least 75 days before the NDI is introduced or delivered for introduction into interstate commerce, information that is the basis on which the manufacturer has concluded that a dietary supplement containing the NDI will reasonably be expected to be safe. DDSP reviews such information to determine whether it is complete and whether DDSP has any questions about it. More generally, DDSP is responsible for taking or recommending action against any unsafe dietary supplement or dietary ingredient after it reaches the market and in doing so DDSP performs assessments on the safety and potential hazards of the use of supplements and ingredients.

Contaminants- CFSAN oversees the safety of the U.S. food supply including both domestic and imported foods. This is performed, in part, through the Center's monitoring programs for a range of pesticides and for industrial chemicals, such as dioxins, polychlorinated biphenyls, and benzene; for chemical contaminants produced in food during processing (e.g., heating) of food, such as acrylamide, chloropropanols, and furan; and for metals and elements in the environment, for example, arsenic, lead, and calcium. Other chemical contaminants of foods include natural toxins such as mycotoxins (e.g., aflatoxin, fumonisin) and chemicals produced by food plants such as hypoglycin produced in the tropical fruit ackee. DRA is responsible for performing the assessment of potential exposure and the hazards and risks posed by these chemicals when contaminants are detected in food commodities.

Cosmetics- Cosmetic products and ingredients are not subject to FDA premarket approval, with the exception of color additives. However, FDA can pursue enforcement action against products on the market not in compliance with the Food, Drug, and Cosmetic Act, or against firms or individuals who violate the Federal Food, Drug, and Cosmetic Act or the agency's regulations. Companies and individuals who manufacture or market cosmetics have a legal responsibility to ensure the safety of their products. FDA has consistently advised manufacturers to use whatever testing is necessary to ensure the safety of their products and ingredients. Firms may substantiate safety in a number of ways.

METHODOLOGY USED FOR THE OFVM CHEMICAL SAFETY ASSESSMENT REVIEW

The OFVM chemical safety review information gathering phase, which took place over the course of approximately 12 months, consisted of the following three parts:

- Anonymous and confidential interviews by Versar, a consulting company, of employees involved in the chemical safety assessment program from both CFSAN and CVM.
- Anonymous and confidential interviews by Versar of CFSAN alumni and senior managers from other Federal agencies.
- Five listening sessions conducted by CFSAN with both internal and external stakeholders on the chemical safety assessment program.

Interviews of CFSAN and CVM Employees- As part of this review, FDA organized interviews of chemical safety assessment personnel working in CFSAN and CVM. For the interview process, interviewees were asked a series of 22 questions: 10 addressing science issues; 7 addressing communication and collaboration within OFVM and with other programs, agencies, and the public; and 5 addressing expertise and training. The questions may be found in the Versar Main Report (Appendix 1).

FDA provided a list of 97 names of personnel involved in the chemical safety program at CFSAN (76 employees) and CVM (21 employees). All potential participants were contacted via email to schedule appointments for interviews. Interviews were conducted with 82 employees from five offices within CFSAN (62 interviewees) and three offices/groups within CVM (20 interviewees). The CFSAN offices included were OAO/DRA, OARSA, OCAC, OFAS, and ONLDS/DDSP. Employee areas of expertise included biology, chemistry, epidemiology, food chemistry, mathematics, medicine, pathology, pharmacology, residue chemistry, risk assessment, and toxicology.

Interviews were conducted under conditions of anonymity and confidentiality by Versar. The following measures were taken to preserve anonymity and confidentiality:

- Individual interviews were conducted in private rooms separate from staff offices;
- Appointments were scheduled on the basis of availability only and were not grouped by program office;
- Appointments were generally separated by sufficient time that an interviewee exiting an interview was unlikely to encounter an interviewee arriving for the next interview; and:

- Each interviewee was assigned a number, and the interviews were stored by number only; relevant comments, thoughts, and quotes were extracted from the individual interviews into a report skeleton with no attribution other than office, center, or area of expertise where it was felt to be relevant. A redacted copy of the report skeleton may be found in Appendix 2.

Written summaries and recordings of individual interviews were maintained by Versar, and were deleted on delivery of the final report of the interviews.

Interviews with CFSAN Alumni and Other Federal Agency Senior Managers- Versar interviewed outside individuals, including CFSAN alumni and senior managers from other Federal agencies with chemical safety assessment and management programs. These external interviews were conducted to augment the results from interviews of the FDA scientists, providing additional insight and perspectives on FDA's chemical safety program. FDA provided lists of names of potential participants for the interviews. All potential participants were contacted via email to schedule appointments for interviews. The interviews were conducted in person, by phone, or by filling out the questionnaire and submitting it via email. Interviewees were asked a series of eight to ten questions addressing topics on science issues, communication and collaboration, and expertise and training. The questions can be found in the Versar report. Versar's report of these interviews may be found in Appendix 3 to this Report.

Listening Sessions-CFSAN/CVM/OFVM held five listening sessions on the chemical safety assessment program. One session was with CFSAN epidemiologists and biostatisticians to learn how these disciplines can be better integrated into the chemical safety assessment process at CFSAN. Two sessions were held with representatives from the food industry and trade associations. Two sessions were held with representatives from different consumer organizations. The topics discussed were in three broad areas: Science Issues, Forecasting Emerging Areas of Concern, and Collaboration/Communications Issues. The report of these listening sessions may be found in Appendix 4 to this Report.

Reports- The results of these interviews were written up in four separate reports:

- FDA Foods Program Review of Chemical Safety Capacity and Management: Results of Chemical Safety Assessment Personnel Interviews (Versar Main Report) (Appendix 1)
- FDA Foods Program Review of Chemical Safety, Capacity, and Management Report Skeleton (Appendix 2)
- FDA Foods Program Review of Chemical Safety Capacity and Management: Results of External Interviews (Appendix 3)
- Results from the Listening Sessions that CFSAN/CVM/OFVM Conducted as Part of the Chemical Safety Assessment Review (Appendix 4)

Outside Consultant Review- Four outside consultants, all of whom had previously held senior management positions dealing with chemical safety assessment in the Federal government and who are currently considered as experts in the field, were asked to participate in the review. The four consultants met with OFVM and CFSAN senior managers and Versar to discuss the results of the interviews and listening sessions. These consultants then reviewed the above documents and gave OFVM and CFSAN written recommendations, which may be found in Appendix 5 to this Report.

Formation of a CFSAN Chemical Safety Review Working Group- At the direction of the Center Director, CFSAN formed an internal Working Group to review all the reports and consultant recommendations. The goal of this review was to develop a report containing prioritized recommendations for improving the chemical safety program at CFSAN, along with a plan for implementing the recommendations.

The Working Group had representatives from OAO/DRA, OARSA, OCAC, OFAS, and ONLDS/DDSP. It was chaired by the Senior Advisor for Toxicology, Senior Science Advisory Staff, in the Office of the CFSAN Center Director. After an initial meeting to discuss the charge to the group, the Working Group divided into three subgroups to consider issues:

- Science Subgroup
- Communication and Collaboration Subgroup
- Training and Expertise Subgroup

Each subgroup looked at all the interview, listening session, and consultant reports and listed its comments and concerns regarding that subgroup's particular issues. The following charge was given to each subgroup:

- Prioritize issues with rationale (metrics) for priority order.
- Provide a statement to describe each issue.
- Describe the impact of the issue on the chemical safety program.
- Include, if possible, at least one short term, one intermediate term and one long term recommendation for each issue.
- Tie its recommendations to recommendations from the reports.

Each subgroup generated a report on major issues, and recommendations that have the potential for improving the CFSAN Chemical Safety Assessment Program. Each group prioritized according to a method developed by its group members. The metrics used by each group may be found in Appendix 6 to this Report. The Issues Section of each subgroup report describes each

of the important issues that were identified, why the issue is important, and how it could affect the chemical safety review programs in CFSAN. The Recommendations Section lists in descending priority order recommendations to address each of the issues.

Each recommendation has been characterized according to the time it would take to implement-short-term (3-6 months) (ST), medium-term (6-18 months) (MT) or long-term (greater than 18 months) (LT). Where possible, each recommendation was also characterized by an estimate of whether it would be resource light (RL), resource medium (RM) or resource heavy (RH). Resources included both monetary and personnel time.

RESULTS

SCIENCE SUBGROUP REPORT

The Versar Main Report identified a very large number of scientific issues (i.e., new methods, nanotechnology, botanical and supplements, endocrine disruptors, mixtures, post-market review, low dose/long term exposure, and additional issues). The Science Subgroup considered this information and identified six major scientific issues, each with several sub-components. The following is a prioritized list of the six science issues identified by the subgroup in descending order of importance:

- *In silico* Chemical Safety Signal Detection Knowledgebase Initiative
- Database Availability / Information Gap
- Scientific Meetings
- Peer Review
- Post Market Review
- Transparency/Consistency of Risk Assessments/Safety Assessments

Issue #1- *In silico* Chemical Safety Signal Detection Knowledgebase Initiative

In silico refers to information obtained using a computer or via computer simulation, in contrast to information obtained from biological systems (*in vivo, in vitro,* and *in situ*).The phrase *in silico* signal detection is used to encompass both the early identification of emerging hazards/risks and prioritizing "older" or "known" risks for reassessment. This phrase was not mentioned in the Versar Main Report; it was created by the subgroup because it conceptually captures a large portion of the science issues described in that report.

Most of the science issues mentioned in the report imply that CFSAN needs to develop a strategy (policy) that allows the Agency to proactively identify and rank emerging hazards, risks, and new science into an *in silico* knowledgebase. This knowledgebase can also be expanded to include "older" or "known" chemical risks for reassessment. CFSAN's premarket risk assessment methods work well for a small number of singular petitioned substances, but it is impractical to apply these methods for every chemical under CFSAN's regulatory jurisdiction.

CFSAN could develop an *in silico* detection knowledgebase that utilizes large sets of available chemical safety data from diverse sources independent of their intended application (e.g., food, drug, cosmetic). The chemical safety signal detection initiative's mandate would be to develop a knowledgebase with predicative tools that can identify and rank the risks of food and cosmetic chemicals regulated by CFSAN.

From a conceptual and toxicological point of view, *in silico* strategies and methods for the rank ordering of chemicals according to estimated toxicities are well established screening tools in the pharmaceutical arena. For example, pharmaceutical companies routinely use quantitative structure-activity relationship software programs to screen combinatorial libraries of millions of chemical structures in order to identify a small number of lead candidate compounds with desirable properties. These programs calculate a wide variety of absorption, distribution, metabolism, excretion, and toxicity (ADMET) and pharmacological properties of the organic chemicals found in the library. Then the programs filter the results to identify chemicals that have the best spectrum of bioavailability or ADMET properties for the intended clinical indication but without specific pharmacological activities.

The aim of an *in silico* Chemical Safety Signal Detection Knowledgebase Initiative approach is to apply the same strategy and related software programs to identify food and cosmetic chemicals that are most likely to be non-toxic and safer for their intended use. However, this would be achieved by reversing (inverting) the paradigm characteristics in the methodology now commonly used to select desirable drug candidates for their pharmaceutical effects to one with minimal toxicological effects. This approach would lead to identifying groups of the safest ingredient or chemical agents in food and cosmetic products for further extensive evaluation.

The biggest impact, along with the greatest advantage, of creating an *in silico* Chemical Safety Signal Detection Knowledgebase Initiative would be the ability to acquire and process *in silico* ADMET safety data for large sets of data poor chemicals in a very short time period. The resulting ADMET data records would provide a robust profile of *in silico* safety data that could be made available to CFSAN scientists to better prioritize specific groups of chemicals for further examination.

Recommendations for *In Silico* Chemical Signal Detection Knowledgebase Implementation:

- Determine which CFSAN group, Division and/or Office will implement, conduct and/or manage (or the administrative location of) the signal detection *in silico* activities. (ST)

- Develop or organize a specialized team of CFSAN chemists and toxicologists with computational toxicology expertise (*i.e.*, Signal Detection Team) to address and perform computational signal detection *in silico* activities and act as core leads in this work. (ST)

- Ensure that the results of the signal detection *in silico* research and data are readily available for CFSAN scientists through the knowledgebase. (LT)

Issue # 2-Database availability / Information gaps

A wide range of data is crucial to the evaluation of chemical safety. Examples of the types of data that are employed to conduct these assessments include adverse effects or events data, toxicological dose-response data, exposure or consumption data, chemical levels in food, migration data, and *in silico* quantitative and QSAR data. The importance of having available verifiable quality data and sufficient access to information from databases was emphasized in the Versar Main Report. The strength and reliability of hazard identifications and safety/risk assessments conducted for chemicals depend on the adequacy and quality of the various types of data and information employed in the review process. Thus, limitations in the availability of quality data, and access to databases were identified as potentially problematic to conducting many essential aspects of chemical safety evaluations not associated with a premarket submission (e.g., food additive, color additive, food contact notification).

Several contributing issues or obstacles were identified or discussed in the Versar Main Report as important factors in the availability to databases. They included:

- Gaps in the staff's knowledge about what data sources were available;

- Limited access to primary or raw data versus summary data;

- Restricted access to data due to confidentiality or proprietary issues;

- Limited sharing of data from other Federal agencies or departments, international bodies or other outside sources (*e.g.*, stakeholders, academics); and

- The need to confirm the accuracy or quality of data.

Addressing these aspects of the data availability and information gap issues are important for continuing to advance the strength and reliability of chemical safety evaluations by CFSAN.

Recommendations for Database availability/Information gap in the Chemical Safety Program:

- Survey CFSAN toxicologists and chemists on specific data sources and databases that they currently use and those they would like access to use. (MT)
- Examine and address issues associated with the obstacles and barriers to data sharing. (MT)
- Organize and list various data sources and databases of use to the chemical safety review program in one location on the CFSAN intranet website. Include staff contact information of those responsible for a database if direct access to the database by all staff is not available. (MT)
- Create a CFSAN liaison contact or position to establish relationships with other Centers, HHS agencies, Federal agencies/departments/groups to explore what data are available and to facilitate access (*e.g.*, possibly MOUs) to these other data sources for CFSAN staff. (MT)
- Explore or develop new sources of exposure-related data such as additional chronic consumption information, consumption by susceptible or sensitive subgroups or subcultures, label information, consumer and market survey data. (MT)
- Address consistent accuracy and quality problems with data collected or generated by different programs, including those in CFSAN, ORA and field labs, and reported in databases used by CFSAN. (MT)

Issue #3- Scientific Meetings

Issues related to scientific meetings often mentioned were: 1) funding limitations; 2) opportunities to attend meetings without the requirement of presenting a paper or poster; and 3) the lack of internal CFSAN chemical safety symposia or conferences. In general, it was recognized that attending scientific meetings is essential for scientists in chemical safety assessment to maintain their expertise, develop contacts in the field, and keep abreast of new developments in the field.

Funding limitations were a common issue related to scientific meetings, making it more difficult to attend meetings. In addition, interviewees noted that it was more difficult to attend meetings due to the requirement that persons attending be invited or presenting a paper. The organization of internal CFSAN symposia, such as "hands-on workshops with some of the emerging

technologies" may assist in maintaining expertise and keeping abreast of recent developments in the field. Together the reports indicated that a lack of opportunities to attend scientific meetings were a serious concern.

Recommendations for Scientific Meeting Implementation:

The most straight-forward way to address these issues would be to increase funding for travel to scientific meetings, and to allow flexibility in the requirements for attendance (such as allowing more scientists to attend meetings without requiring presentations). However, the subgroup recognized that increasing funding or allowing more flexibility for travel to attend scientific meetings may not be possible with the current travel budget constraints and Executive Branch travel policies. Thus, the subgroup discussed several options to increase the opportunities for CFSAN scientists to participate in scientific meetings, including:

- Increase the use of webcasting and partnering with outside stakeholders; (LT)
- Establish an "electronic bulletin board" of free webcasts, local meetings, etc.; (MT)
- Organize more internal symposia and conferences; and (LT)
- Enhance knowledge of and access to courses given by other FDA Staff Colleges. (ST)

Issue #4- Peer Review

Peer review is a mechanism by which experienced and qualified colleagues and/or experts contribute to the steps and/or outcome of the evaluation and regulation of the safety of a chemical. It is a review process that allows for feedback on aspects of chemical safety/risk assessments that may include the interpretation of data or findings, decisions, points of focus, or work products. In some instances, it may encompass engagement of and/or general feedback or commenting from stakeholders on aspects of CFSAN work and focus.

The process of peer review plays a multifaceted role in the evaluation and assessment of chemical safety in general and in CFSAN's chemical safety program in particular. First, it provides a mechanism that serves to ensure that CFSAN chemical safety work products achieve scientific adequacy, accuracy, and consistency via the review and feedback of and exchange with peers. Second, it serves as a tool for educating new or junior science staff on aspects of the approaches employed for regulatory-related chemical safety evaluation at CFSAN, and for safety/risk assessment in the field of toxicology. Lastly, the peer review process serves as a way to engage outside experts, various stakeholders and the public leading to receipt of independent feedback, and improved transparency, accountability, communication, and delineation of issues for the Center.

Two principal types of peer review were acknowledged and addressed in the Versar Main Report, "Internal Peer Review" and "External Peer Review." Internal peer review involves the role and contribution of peer review in the internal review process for science evaluations of chemical safety performed within CFSAN. Relevant components of this process are the avenues for gaining supplemental critical reviews of work and related interpretation of data, and for allowing increased communication and exchange from additional individuals or teams of expert toxicologist(s), chemist(s) or other scientists.

The overall goals of internal peer review were described as improved scientific interpretation, adequacy, and decision-making and better quality assurance and more sound science in the approaches used and of the work products. Although some indicated improvements and consistency are needed in various aspects of this review process, the majority of interviewees believed that there are generally established processes and acceptable procedures in place to implement internal peer review.

The other principal type of peer review is external peer review. This process was considered important for CFSAN to obtain feedback from and critical evaluation by outside scientific experts on specific major work products and activities such as safety or risk assessments, methods evaluations, data interpretation, approaches taken, and the tentative conclusions associated with these assessments, evaluations, interpretations, and approaches. The Center's current use of external expert(s) from other Federal agencies or expert panels to review and provide feedback on CFSAN assessments or other work products was considered an underutilized resource in the Center's external review process.

Another important aspect of the external peer review process was to expand or enhance the use of various types of advisory committees (e.g., science advisory committees or panels, program dialog committees) and convening meetings of them on a regular basis to receive external input in a proactive manner.

Expanding and enhancing both internal and external peer review will increase transparency, accountability, and the scientific rigor and integrity of CFSAN's chemical safety/risk assessments.

Recommendations for Peer Review Implementation

Internal Peer Review Process

- Promote increased peer review by additional Center expert toxicologists or chemists, or by internal expert cross-organizational teams if warranted by the nature of project or if requested. (ST)

- Establish an option for additional supplemental internal peer review within the established processes in place and currently implemented for chemical safety/risk assessments (*e.g.*, current processes: first line supervisors; secondary source: higher level management for larger issues). (ST)

- Promote the development of mechanisms and forums that increase communication and exchange among toxicologists to improve and encourage scientific excellence, understanding, and consensus, and thus consistency in CFSAN's chemical safety/risk assessments. (MT)

- Establish mechanisms within the internal peer review process to achieve consensus or decision-making resolution if differences in the interpretation in data and findings and/or conclusions occur. The CFSAN lead or Office responsible for conducting the assessment should have responsibility for resolving any differences in scientific opinion and completing the assessment or evaluation. (MT)

- Develop a system or options for improved internal peer review for work products prepared by staff that utilized an integrated review team approach. (ST)

External Peer Review Process

- Continue to engage in the external peer review process to get feedback and critical analysis from outside expertise on major safety/risk assessments and other key work product and approaches (*e.g.*, external experts, expert panels, science advisory committees). (MT)

- Periodically publish (e.g., every 5 years) a list(s) of relevant and priority chemicals with brief reviews of the hazards and issues associated with them. (LT)

- Engage with other Federal agencies and leverage their scientific expertise in the external review process at CFSAN. (MT)

- Use public meetings, webinars, and conferences early in the process of the assessment of certain chemicals and their toxicological hazards. (LT)

- Organize balanced science advisory committees or panels of independent and objective scientific experts to provide advice and recommendations on FDA programs, new scientific methodologies, risk assessments and related paradigms, etc. and hold regular public meetings concerning their feedback. (LT)

- Consider establishing a food chemical safety program dialog advisory committee comprised of a diverse group of stakeholders representing non-governmental organizations (NGOs), state governments, other Federal agencies, trade organizations, product users, etc. similar to the EPA Pesticide Program Dialogue Committee (http://www.epa.gov/pesticides/ppdc). (LT)

Issue # 5- Post-Market Review

There are two separate situations in which post-market chemical safety/risk assessments are performed by CFSAN. In some operating units (e.g., OAO/DRA), post-market review is standard practice. In OFAS, where products are typically reviewed in a premarket setting, post-market review is performed in addition to Congressionally-mandated premarket review.

Recommendations for Post-Market Review Implementation:

- Assign dedicated personnel for post-market review in Offices where there currently is no dedicated staff for such review. (RH, LT)
- Address workload stress through altered management of assignments by team leaders because some of the workload stress comes from the fact that the post-market review is assigned in addition to other tasks in some CFSAN Offices. (RL, ST)

Issue #6.-Tranparency/Consistency of Chemical Risk Assessments/Safety Assessments

The Science Subgroup believed that issues surrounding the consistency of safety/risk assessments could be divided into three sub-issues:

- Differences in the statutory paradigm for different programs (e.g., food additives, dietary ingredients, contaminants);
- Ensuring internal consistency of safety/risk assessments within CFSAN.
- Harmonization of methodology, where possible. The subgroup defined harmonization within CFSAN as achieving consistency in how studies are used and data are interpreted across CFSAN.

The Versar Main Report indicated that those involved in chemical safety review in CFSAN wanted consistency of approach, at least within program areas. There was agreement that consistency within a program area was achievable. Consistency in methodology across program areas may also be achievable; for example, consistency in conducting and interpreting the results of a particular genotoxicity assay.

Recommendations for Transparency/Consistency of Chemical Safety/Risk Assessments:

- Determine to what extent consistency on the methodology used for chemical safety/risk assessment between and across offices at CFSAN and between CFSAN and CVM is achievable. (MT)

- Develop SOPs to help ensure consistency within CFSAN Offices on chemical risk assessments/safety assessments. (LT)

COMMUNICATION and COLLABORATION SUBGROUP REPORT

The subgroup identified the following four main issues regarding communication, collaboration, and coordination, prioritized in the following order of importance:

- Effectiveness of communication within CFSAN and between CFSAN and other FDA Centers
- Collaboration within CFSAN and between CFSAN and other FDA Centers
- Interaction with other Federal agencies and international bodies
- Coordination of laboratory research to support CFSAN priority chemical safety/risk assessments

Issues #1 and #2- Effectiveness of communication within CFSAN and between CFSAN and other FDA Centers, and Opportunities for collaboration within CFSAN and between CFSAN and other FDA Centers.

The Versar Main Report clearly indicated that a substantial number of the chemical safety assessment staff believe that: (1) there is insufficient communication between research staff and reviewers, across working groups, Divisions, Offices, and CFSAN and CVM; (2) there is a need for SOPs that detail accepted procedures to establish formal collaborations; (3) a subject matter expertise database should be developed within CFSAN and CVM.

Successful existing coordination/collaboration efforts depended on the personnel involved and were often the result of individual initiatives, with few formal processes. Management neither discouraged nor supported collaborations except for major issues and large projects. External collaboration opportunities were more difficult to initiate because of time and travel restrictions, restrictions in the way FDA relates to industry, and regulations governing clearance/approval processes of collaborations. Overall, collaboration initiatives within and between CFSAN and CVM lacked a formal process.

The Versar Main Report highlighted the following general needs related to communication and collaborations across Offices within the Centers:

- Better and increased communication across Offices and groups;
- Better communication within and between CFSAN and CVM;
- Formal SOPs on how and when collaborations should occur;
- Increased inter-group meetings and informal discussions among staff and managers; and

- Increased support and buy-in from CFSAN upper management regarding proposed changes related to collaboration and communication.

Better collaboration and communication among those involved in chemical safety/risk assessments would have many benefits for the program including:

- Improved ability to be proactive overall, especially in post-market surveillance activities;
- Improved ability for CFSAN and other FDA Centers to achieve goals for domestic and global harmonization of standards;
- Increased/improved scientific transparency (internally and externally) and serving as a "think tank" for implementing innovative ways of data-sharing;
- Improved accessibility to scientific /regulatory information;
- Improved efficiency in identifying cross-cutting emerging scientific and regulatory issues, in addition to identification of chemicals with emerging safety concern;
- Better utilization and leveraging of staff and financial resources;
- Better understanding of new technologies that could lead to the Center's use of improved, simplified risk assessment procedures for chemicals;
- Increased opportunities to highlight and promote ongoing efforts within CFSAN and foster a better understanding of various chemical safety/risk assessment tasks within CFSAN and across CFSAN and CVM;
- Enhanced visibility of FDA in the scientific community.

Recommendations for Communication:

Manager/Manager Communications:

- Establish more frequent communications between senior managers so they know each other and understand respective work priorities. Meetings will foster communication and collaboration across offices in CFSAN as well as with CVM and other FDA Centers. (ST, RL).

Manager/Reviewer Communications:

- Establish routine meetings between managers and with staff as opportunities to discuss work-related matters, work priorities, and regulatory decisions including:

- Develop formal processes for engagement between CFSAN programs in each operating unit. (LT, RH)
- Hold routine all-hands operating unit meetings for staff. (ST, RL)
- Continue the routine CFSAN Director monthly all-hands meetings and explore the possibility of increasing these Center-wide all-hands meetings. (ST, RL)
- Develop a lead manager for each CFSAN scientific discipline (e.g., chemistry, toxicology). This person could lead and monitor this communication effort among the review scientists within his/her discipline. The lead manager would periodically meet and report on significant communication/collaboration accomplishments. The lead managers would also report to management. (MT, RM)
- Hold routine meetings among Team Leaders in each Office; periodic meetings among Team Leaders within Offices in CFSAN; periodic (biannual) meetings among Team Leaders across Offices in CFSAN and across CSFAN and CVM. (ST, RL)

Reviewer/Reviewer Communications:

- Establish routine meetings between reviewers across programs in Offices in CFSAN as a means to foster communication. (ST, RL)
- Establish teams of review scientists from various disciplines to discuss focused scientific or regulatory goals/issues as a way for problem-solving. (ST, RL)
- Enhance communication among reviewers in CFSAN and CVM. This initiative would educate reviewers regarding similar review processes between CFSAN and CVM; facilitate the sharing of similar SOPS; and may foster exploring ways for data sharing. (MT, RM)

Recommendations for internal collaborations:

- CFSAN should develop general guidelines for when to engage various scientific disciplines in particular types of matters. (LT, RH)
- Each operating unit in CFSAN should establish formal SOPs for collaboration processes specific to its responsibilities, for example, SOPs pertaining to who initiates collaborations and when collaborations are initiated. (LT, RH)
- Enhance and increase detail opportunities for staff. (LT, RH)

- Operating units should initiate more ways to share data and information, including memos within as well as across Offices and posting of final regulatory memos on the CFSAN intranet website. (MT, RM)
- Operating units should post final memos in support of a major safety/risk assessment on CFSAN intranet websites. (ST, RL)
- Operating units should establish a CFSAN expertise database to facilitate appropriate team formation and to identify SMEs within CFSAN and FDA. This would provide transparency in identifying expertise within CFSAN and FDA. (ST, RL)
- Institute regularly meetings to facilitate planning and information exchange between different levels of management and different types of staff (ST, RL):

    - Within each operating unit, managers/supervisors should establish routine meetings with reviewers/researchers as opportunities to discuss work-related matters, work priorities, and regulatory decisions.
    - Within each operating unit, managers/supervisors should hold all hands meetings for all staff.
    - Senior managers in CFSAN and other Centers should meet periodically to better get to know each other and understand their respective work priorities with a view toward fostering communication and collaboration across operating units in CFSAN as well as CVM, and other FDA Centers and Offices.

Recommendations for external collaborations:

- Increase collaborations between CFSAN review scientists and academia. (LT, RH)
- Announce (publicize) publications from CFSAN Staff on the CFSAN and FDA websites. (ST)

Issue #3- Interactions with other Federal agencies and international bodies.

The Versar Main Report indicated that CFSAN interacts with many other Federal agencies and organizations. Interactions were variously described as "close relationships; effective but affected by priorities; occurring when necessary and when law and regulations demand; occurring at all levels for significant issues; more effective when initiated at higher levels; limited to designated people selected by management; not occurring as frequently as they should; and virtually nonexistent at the staff level."

The input obtained from the external interviews of FDA alumni and other agency managers and the reports of outside consultants are largely consistent with the wide diversity of opinions

obtained from the Versar Main Report. Examples mentioned by FDA alumni and other agency managers of specific issues in which substantial interaction between FDA and other agencies occurred include: mercury in seafood; biotech foods; non-monotonic dose-response for endocrine active chemicals; Tox 21; and arsenic in rice and rice products.

The benefits of increased external coordination and collaboration include:

- Ensuring that regulatory action by one agency on a chemical safety issue that might affect another agency does not catch the other agency unaware;
- Increasing efficiency and leveraging of resources as resources become constrained; and
- Ensuring joint preparation of public communications so that the conclusions of one agency on an issue do not vary or appear contradictory to those of another agency.

Recommendations for interactions with other Federal agencies and international bodies:

- Encourage upper management at OFVM and CFSAN to hold regular meetings with counterparts at other agencies to identify common issues where coordination / collaboration should occur. (MT, RL)
- Identify appropriate CFSAN SMEs to work with scientists at other agencies on important common issues. (MT, RL)
- Consider SME details/exchanges between agencies. (LT, RH)
- Explore where MOUs (or other ways of sharing of information between agencies) should be implemented to facilitate collaborations. (MT, RM)

Issue #4- Coordination of laboratory research.

Many issues regarding coordination of laboratory research by CFSAN, CVM, and NCTR were identified in the Versar Main Report. Approximately half of the interviewees believed that coordination/collaboration was poor or needed to be improved.

There were three different areas where improvements were needed:

Manager/Manager Communication

- Need for CFSAN Senior Managers to meet periodically to share identified current and future research priorities regarding crosscutting scientific issues. Set up long-term (2-3 years) plans for work tasks. This would identify common proposed goals and then foster collaboration and communication across CFSAN and CVM.
- Need for senior managers to better get to know each other and understand priorities.

Manager/Researcher Communication:

- Few formal processes exist; need formal SOPs on how collaborations should occur.
- Need for better communication between NCTR and OARSA and CVM's Office of Research.
- Need for SOPs for how NCTR and OARSA should interact on projects.
- Need for better coordination of research activities to prevent any overlap.
- Need for immediate training session for all scientific (research) and regulatory staff regarding procedures for requesting and implementing NCTR research projects including how scientific projects are chosen for NCTR. Need to find better ways to disseminate NCTR information. Only a few FDA staffers sit on NCTR panels.
- Collaboration is "not valued" and is sometimes discouraged.

Researcher/Researcher Communication:

- Difficult to find people working on same topic/do not know what others are working on.
- Need to identify expertise within CFSAN as well as identify external expertise in other FDA Centers to identify possible collaborators.

Recommendations for coordination of research:

- Encourage CFSAN senior managers to meet periodically to share identified current and future research priorities regarding crosscutting scientific issues. Set up long-term (2-3 years) plans for research tasks. This would identify common proposed goals and then foster collaboration and communication across the CSFAN and CVM. (MT)
- Develop a list of individuals and their documented research expertise. This could be incorporated into a CFSAN internal expertise database which could be searched to find individuals with specific expertise. CFSAN leadership could contact the other Centers within FDA to determine if similar databases exist and to discuss either combining them or developing a method to search them. (ST, RL)
- Develop a mandatory training course for all chemical safety review staff and laboratory researchers which provides a detailed explanation and overview of the laboratory research coordination process. (LT)
- Establish SOPs for research collaborations between CFSAN and the National Center for Toxicological Research and NTP and ensure that all researchers receive training on the SOPs. (ST)

EXPERTISE AND TRAINING SUBGROUP REPORT

Expertise and training are closely related issues which together contribute substantially to the success of the Center. Several CFSAN senior chemical safety scientists are at or within five years of retirement eligibility, suggesting the imminent loss of institutional knowledge, expertise, and leadership. Maintaining subject matter expertise requires support in the form of time and fiscal resources as well as an organizational culture that fosters growth and development.

Employees should be regarded as a vital resource, whose expertise should be nurtured in order to maintain state-of-the-art knowledge and information about current scientific developments. Nurturing their expertise will help ensure that they keep abreast of compounds or issues of emerging concern and be trained and educated in new technologies and methods. Such commitment would improve CFSAN's ability to shift from reacting to anticipating.

The subgroup identified the following issues in order of importance:

Expertise

- Need to identify current SMEs;
- Need to effectively utilize and develop current SMEs;
- Need to identify current and future areas of needed expertise;
- Need to maintain expertise.

Training

- Need to identify best practices for training;
- Need to increase resources for training;
- Need to identify and develop training opportunities.

Expertise

Issue #1 Identify Current SMEs

CFSAN does not have a clearly identified method for identifying and tracking SMEs including those within CFSAN, within FDA, or other Federal government agencies, including advisors with government clearance, and those experts outside of government. Areas where improvement is needed are:

- Expertise in recruiting and hiring chemical safety scientists to better enable CFSAN to locate and then attract qualified personnel to government vs. industry, to address emerging issues (e.g., Tox21);
- Retaining expertise in areas of emerging technologies;
- Utilizing available expertise: Due to lack of an effective system for identifying and locating expertise within CFSAN and CVM and lack of communication, coordination, and collaboration between Offices and Centers, CFSAN and CVM cannot maximize the use of existing expertise;
- Defining and vetting expertise: An expert should have an in-depth understanding of both the well-settled and emerging aspects of an area, not just an area of interest; and vetting of experts must go beyond their publication record, as publications alone are not always sufficient to determine that a scientist can function in a chemical safety program; and
- A small number of SMEs in a single area, sometimes referred to as a lack of "bench strength," increases the Center's vulnerability to the adverse institutional effects of retirements or departures for other reasons. Further, the demands on a small number of SMEs in a single area may not allow for sufficiently thorough peer review.

Areas of greatest current expertise include chemistry, toxicology, biology/medicine, environmental science, nanotechnology, exposure/safety/risk/hazard assessment, analytical methods, mathematics, food sciences, and regulatory affairs.

Areas of where CFSAN needs to increase its expertise include industrial chemistry, renal toxicology, toxicogenomics, mixture toxicology, metabolism, and food packaging toxicology; developmental biology, modern biochemistry, biological systems modeling, pharmacology, pharmacokinetics and modeling, epigenetics, mechanisms of carcinogenesis, physiology, genetics, proteomics, interspecies extrapolation, gastroenterology, pathology, oncology, neurology, and stem cells research; interaction between *in vitro* and *in vivo* models, high throughput methods, analytical methods development, data analysis, and scientific and technical writing and editing.

Recommendations for Identification of SMEs:

- Develop a better method(s) of identifying, tracking, and engaging SMEs within CFSAN and CVM and FDA (ST, RL):
    - One proposed method of addressing this issue is to improve, publicize, and mandate employees to use the Science First webpage, an easy and relatively quick solution to implement;

  - An alternative approach is the identification of in-house subject matter experts through use of a social network (i.e., LinkedIn) searchable database;
  - Compiling, centralizing, and publicizing a list of in-house subject matter experts (e.g., Excel spreadsheet);
  - SOPs in place to identify contacts and subject matter experts; and,
  - Improving identification of contact persons within other offices, centers, and agencies, to collaborate on emerging issues.

- Develop better method(s) of identifying, tracking, and engaging SMEs with other government agencies; (MT), and
- Develop better method(s) of identifying, tracking, and engaging experts outside of government. (LT)

Issue #2 - Effective Utilization of Current SMEs:

It appears unlikely that expertise within the Center is used to its full potential, due to the lack of communication between and among Offices and between CFSAN and CVM, and the lack of a system for identifying current SMEs in CFSAN and in other Federal agencies, and outside of government.

Recommendations for Proper Utilization of SMEs:

- Fostering Interaction of SMEs across the Center by: (ST-MT)
  - Increasing the use of integrated teams to address specific issues and special projects;
  - Increasing flexibility in deployment and use of staff;
  - Improving communication, integration, and interaction across Offices and Centers including between labs and regulatory personnel;
  - Using matrix management to prevent "Stove-piping" and "pigeon holing"; and,
  - Enhancing the level of staffing and adjusting workloads to allow time to work on emerging issues.
- Promoting collaboration with outside scientists via seminars, workshops, symposiums.
- Increasing outreach with industry, trade associations, and scientific community to get expertise in timely manner.

Issue # 3 – SME Identification of **Current and Future Needs of SMEs**:

Safety/risk assessment practice in CFSAN requires scientists with diverse backgrounds. Because of advances in laboratory technology as well as computer science, the science of toxicology is currently undergoing a major paradigm shift with regard to how both wet and dry laboratory toxicology is practiced.

SMEs and their supervisors must be responsible for identifying appropriate training and continuing education opportunities to maintain and advance their expertise, for example, with respect to new developments in safety/risk assessment. SMEs and their supervisors should incorporate training needs into their performance plans and assessments of performance related to accomplishing the training goals should be conducted at mid-year and end-of-year reviews.

Recommendations to Identify Current and Future Needs of SMEs:

- SMEs and their supervisors should identify, and SMEs should attend, appropriate training and continuing education courses periodically/on a regular basis; (MT, RM)
- SMEs should document training and continuing education courses completed. (ST, RL)

Issue # 4 -CFSAN Role in Maintaining and Advancing Expertise

The Versar Main Report indicated that although the scope of expertise within CFSAN is adequate to fulfill current regulatory obligations, having only one SME in an area increases the Center's vulnerability to the adverse institutional effects of retirement and departures for other reasons. Further, the demands on a small number of SMEs in a single area may not allow for peer review and sufficient thoroughness. In addition, the requirements for maintaining and continuance of the subject matter expertise are unclear.

Once SMEs are identified and recruited, CFSAN should ensure their continuing education and training. The Center must provide sufficient opportunities to maintain and advance expertise through expansion of professional development opportunities such as attending scientific conferences, meetings or specialized in-house or external training that meet the needs of the identified SMEs and broader training that provides for the maintenance of a broad category of SMEs (e.g., toxicologist, chemist). Scientists who have been awarded expert status either through FDA Peer Review Panel or the Center's Master Reviewer Panel should be provided clear criteria for the cyclic review of their expert package in order to help them develop a training program (i.e., Individual Development Plan) to fit their expertise and maintenance of their expert status. One of the elements of continued professional growth must be, at a minimum,

an annual demonstration, as part of the performance evaluation (e.g., PMAP) process, of training and continuing education taken and completed.

Recommendations for Maintaining and Advancing Expertise:

- Provide SMEs and other CFSAN scientists with the training necessary to maintain and advance expertise in their field; (ST, LT))
- Mandate training and continuing education of SMEs through annual performance plans (e.g., PMAP) unless such training/continuing education was requested but could not be completed because of the unavailability of funds; (ST, RL)
- Develop focused programs to minimize gaps in expertise due to retirements or departures for other reasons; (MT) and
- FDA should work with OPM to update the requirements for the toxicologist series (GS-415) (LT): For example, board certification as a toxicologist or being a Full Member of the Society of Toxicology should suffice.

TRAINING

Issue # 1- Identify Best Practices of Training

The Versar Main Report indicated that CFSAN training needs were not being met. The primary constraint to meeting training needs was funding. Others included time constraints and lack of communication of available opportunities. Maintaining a training budget with proper allocation of funding is essential for CFSAN to remain current with science and with proper long-term planning.

Recommendation for Best Training Practices:

- Look to CVM as a model in identifying best practices of training. (ST)

Issue #2 - Increase Resource Allocations for Training

Resource allocation for training/continuing education involves financial commitment. Resource allocation efforts should take into account not only the training requests but, more importantly, prioritization of the requests by the Offices in meeting their needs. This activity requires clear knowledge of the progress in the relevant scientific field(s) and what is needed that is consistent with immediate Office needs. Increases in funding for training and continuing education and proper utilization of the allocated resource should significantly involve the supervisors and other scientists associated with the SMEs requesting the training. The process should be optimized depending on the Office, its duties and responsibilities and its mission, in keeping with the broader goals of the Center.

Recommendation for Resource Allocation:

- Chemical safety staff and their supervisors should select, or help design, training and continuing education courses, so that resources are allocated to match program needs. (LT, RH)

Issue # 3- Identify and Develop Training Opportunities

There appears to be a lack of communication of training opportunities as well as inadequate identification of training needs. The interest in training goes beyond wanting to maintain expertise in a specific area, but includes interest in learning about what others are doing in other Offices within CFSAN as well as how other Divisions and groups within a Division accomplish their tasks.

Recommendations for Training Opportunities:

- Better collaboration with Staff College to develop science training courses in chemical safety/risk assessment. (MT)
- Better communication of available training (i.e., improve CFSAN Staff College intranet website and search capabilities). (ST)
- Develop a "listserv" for: (ST)
    - Program Office-sponsored continuing-education seminars, webinars, and distance-learning opportunities (e.g.., OARSA Seminar Series, OCAC Brown Bag Seminar Series, OFAS Lunch Seminar Series). This should be cross-cutting for all seminar/webinar series, FDA-wide.
    - Departmental seminars available at local universities and colleges throughout the Baltimore-Washington-Northern Virginia area that would be "accessible" to CFSAN Staff via "local" travel.
    - Local area professional society meetings and national professional society meetings, and encourage staff to attend and become involved with the networking opportunities afforded through affiliation with such societies.
    - Course offerings each semester at area colleges and universities as well as other continuing education opportunities through USDAGS and UNISYS or NIH.
- Consider providing "line items" in Office budgets to support professional society membership dues for scientific staff and to provide for attendance at a minimum of one national meeting per staff member per year, not necessarily contingent on presenting a paper or poster. (LT)
    - Provide for cross-training of CFSAN chemists and toxicologists to better understand each other's needs and methods. (LT)
    - Continue to partner with various Professional Societies to bring training to CFSAN. Consider use of outside contractor organizations such as Center for Professional

Advancement (CfPA) and/or Centers of Excellence as providers of continuing education course opportunities. (LT)

- Provide for details, sabbaticals to academia, other Federal and foreign government agency partners, NGOs, and/or industry.
- Increase hiring to provide flexibility in training opportunities.
- Topics identified for course development include:
    - Pharmacognosy (and natural product chemistry);
    - Biotechnology
    - Nanotechnology
    - Scientific Information Retrieval
    - Computational Toxicology
    - Pathology
    - Microbiology and Molecular Biology
    - Economic "Cost-Benefit Analysis"
    - Environmental Science and Law/Regulation
    - Biostatistics, Epidemiology, and Methods of Data Mining
    - Analytical methods
    - Safety & risk assessment and management
    - QC/QA
    - GLPs/GCPs/GMPs
    - Toxicology
    - Industrial Practices
    - Communications

DISCUSSION AND PATH FORWARD

The Chemical Safety Working Group recognized the significant resources that were expended on this review and the valuable recommendations that resulted and that taken together have the potential to strengthen the CFSAN Chemical Safety Assessment Program.

The Working Group was concerned that without a concrete plan to go forward and to track progress, many of these recommendations would not be acted upon. Therefore, the Working Group believes that it is important for CFSAN to put in place a plan to implement these recommendations in a straight forward, transparent manner so all the people who participated in the review, including employees in the chemical safety program, will see the benefits of their efforts. This implementation plan should include an oversight and/or tracking committee in the Office of the Center Director to ensure that adequate progress is being made.

The Working Group has begun the implementation process by dividing the recommendations into three categories: short, medium, and long-term actions/recommendations. The Working Group believes that with a genuine commitment on the part of CFSAN, all these recommendations are achievable in the timeframes allotted.

Short-Term Actions/Recommendations

The following are recommendations that the Working Group believes can be implemented in CFSAN within 3-6 months and that will have a big impact on the chemical safety program with little expenditure of resources. Details for each of these recommendations are in the Results section of this report.

- Begin to implement an *in silico* Chemical Safety Signal Detection Knowledgebase Initiative by determining which CFSAN group, Division and/or Office will implement, conduct and/or manage (or the administrative location of) the signal detection *in silico* activities.

- Develop a system or options for improved internal peer review among Center colleagues or experts within the same discipline for work products developed utilizing an integrated review team approach.

- Promote increased peer review by additional Center expert toxicologists or chemists, or by internal expert cross-organizational teams if warranted by the nature of the project or if requested.

- Hold routine all-hands operating unit meetings for staff to discuss work-related matters, work priorities, and regulatory decisions.

- Establish a method(s) of identifying, tracking, and engaging experts within CFSAN and elsewhere within FDA.

- Provide SMEs and other CFSAN scientists with the training necessary to maintain and advance expertise in their field

- Look to CVM for a model in identifying best practices of training.

- Create an "electronic bulletin board" of free webcasts, local meetings, etc.

- Organize more internal symposia and conferences on topics relevant to chemical safety.

- Increase access of CFSAN scientists to courses given by other FDA Staff Colleges.

- Provide opportunities for cross-training of CFSAN chemists and toxicologists to better understand each other's needs and methods.

- Require subject matter experts to take continuing education and training courses on a regular basis, and document training/continuing education completed through the annual performance evaluation (i.e., PMAP) process.

- Establish a CFSAN expertise database to facilitate appropriate team formation and to identify SMEs within CFSAN and FDA. This would provide transparency in identifying expertise within CFSAN and FDA.

- Establish SOPs for research collaborations between CFSAN and the National Center for Toxicological Research and NTP and ensure that all researchers receive training on the SOPs.

Medium-Term Actions/Recommendations

The following are recommendations that the Working Group believes can be implemented in CFSAN within 6-18 months that will have a significant impact on the chemical safety program with a moderate expenditure of resources. Details for each of these recommendations are in the Results section of this report.

- Determine to what extent consistency on the methodology used for safety/risk assessment between and among offices at CFSAN and between CFSAN and CVM is achievable.

- Survey CFSAN toxicologists and chemists on specific data sources and databases that they currently use and those they want access to use, and identify obstacles to accessing data and determining their integrity

- Organize and list various data sources and databases of use to the chemical safety review program in one location on the CFSAN intranet website with contact information if direct access is unavailable.

- Create a CFSAN liaison contact or position to establish relationships with other Centers, HHS agencies, Federal agencies/departments/groups to explore what data are available and to facilitate access (*e.g.*, possibly MOUs) to these other data sources for CFSAN staff.

- Promote the development of mechanisms and forums that increase communication and exchange among toxicologists to improve and encourage scientific excellence, understanding, and consensus and thus consistency in CFSAN's chemical safety/risk assessments.

- Establish mechanisms within the internal process for peer review of safety/risk assessments to achieve consensus or decision-making resolution if differences in the interpretation in data and findings and/or conclusions occur. The CFSAN lead or Office responsible for conducting the assessment should have responsibility for resolving any differences in scientific opinion and completing the assessment or evaluation.

- Engage with other Federal agencies and utilize their scientific expertise as a resource in the external review process at CFSAN to get feedback and critical analysis from outside expertise on major safety and risk assessments and other key work product and approaches (*e.g.*, external experts, expert panels, science advisory committees).

- Develop a lead manager for each CFSAN scientific discipline (e.g., chemistry, toxicology). This person could lead and monitor this communication effort among the review scientists within his/her discipline. The lead manager would periodically meet and report on significant communication/collaboration accomplishments. The lead managers would also report to management.

- Increase data and information sharing, including memos within as well as across Program Offices and posting of final regulatory memos on the CFSAN intranet website.

- Encourage upper management at OFVM and CFSAN to hold regular meetings with counterparts at other agencies to identify common issues where coordination/ collaboration should occur.

- Explore where MOUs (or other ways of sharing of information between agencies) should be implemented to facilitate collaborations.

- Develop focused programs to minimize gaps in expertise due to retirements or departures for other reasons.

- Explore or develop new sources of exposure-related data such as additional chronic consumption information, consumption by susceptible or sensitive populations, label information, consumer and market survey data.

Long-Term Actions/Recommendations

The following are long-term recommendations that will require substantial time and resource investments by CFSAN and that will add value to the chemical safety program. The Working Group believes that CFSAN could accomplish these goals within 18 months-4 years. Details for each of these recommendations are in the Results section of this report.

- Develop SOPs to help ensure consistency within CFSAN Offices on chemical safety/risk assessments.

- Examine and address issues associated with the obstacles and barriers to data sharing within CFSAN, with other Centers, Federal agencies and other stakeholders.

- Periodically publish (*e.g.*, every 5 years) a list(s) of CFSAN-relevant and priority chemicals with brief reviews of the hazards and issues associated with these chemicals.

- Use public meetings, webinars, and conferences early in the process of the assessment of certain chemicals and their toxicological hazards.

- Organize balanced science advisory committees or panels of independent and objective scientific experts to provide advice and recommendations on FDA programs, new scientific methodologies, risk and safety assessments, etc. and hold regular public meetings concerning their feedback.

- Consider establishing a food chemical safety program dialog committee comprised of a diverse group of stakeholders representing NGOs, state governments, other Federal agencies, trade organizations, product users, etc. similar to the EPA Pesticide Program Dialogue Committee.

- Assign dedicated personnel for post-market review in Offices where there currently is no dedicated staff for such review.

- Each operating unit in CFSAN should establish formal SOPs for collaboration processes specific to its Office, for example, SOPs pertaining to who initiates collaboration and when collaborations are initiated.

- Continue to partner with various professional societies to bring training to CFSAN.

- Develop a mandatory training course for all chemical safety review staff and laboratory researchers which provides a detailed explanation and overview of the laboratory research coordination process**.**

- Continue to provide SMEs and other CFSAN scientists with training necessary to maintain expertise in their field.

- FDA should work with OPM to update the requirements for the toxicologist series (GS-415): For example, board certification as a toxicologist or being a Full Member of the Society of Toxicology should suffice.

CONCLUSIONS

The Chemical Safety Working Group thanks OFVM and CFSAN Management for the opportunity to participate in this important review of the Chemical Food Safety Program at CFSAN. We believe that implementation of these recommendations will make effective and efficient use of CFSAN's chemical safety resources, ensure the rigor and effectiveness of this program, and maintain and strengthen CFSAN's national and international leadership role in food and cosmetic safety.