

# FDA Foods Program Review of Chemical Safety Capacity & Management Report Skeleton

**Interview Summary:**      **Subject #:** \_\_\_\_\_  
**Center/Office:** \_\_\_\_\_  
**Yrs. exp.:** \_\_\_\_\_

## Overall themes:

(b) (5)

## Science Issues:

- This effort is an outstanding effort by management: very much needed. Now the acid test will be whether they act on it or not.
- It would have been nice to have made the purpose of these interviews clear up front. It would be helpful for the report to recapitulate what the process was for those who weren't part of the process: show the scope of the outreach.
- There is concern over the potential that this survey is part of the plan to merge the centers into a central toxicological office.
- ██████████ has deep expertise in chemical safety and risk assessment that is invisible to other chemical safety programs.  
██████████ has expertise in exposure assessment that seems better integrated with exposure assessment capabilities in ██████████ and ██████████. ██████████ has shrunk to 5 toxicologists two of which have 30+ years of service and could retire at any time and one is within 5 years of retirement eligibility. The group has a tradition of thinking of itself as composed of generalists who learn what is necessary to respond to urgent requests for analysis without reaching out to colleagues elsewhere in the Center or Agency. It is poorly equipped to handle the broad spectrum of contaminants which can be found in food which are its responsibility.

Current staff: years FDA service			No current expertise
<10	20+	25+	(* indicates recent retirement)
Molecular toxicology	Neurotoxicology	Neurotoxicology/ Dose/response modeling Nutritional biochemistry Heavy metals	Renal (Kidney)* Carcinogenesis* PCBs/PAHs /dioxins* Mycotoxins Reproductive toxicology Hepatic toxicology (liver)

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## 1. What do you see your program doing particularly well with respect to chemical safety review or research?

### Responsive to mission

[REDACTED]:

- We do what we need to do. Try to be consistent, science-based
- We do a good job at protecting public health from the perspective of the GRAS program.

[REDACTED]:

- Focus on the task or the job that we are mandated to do, working within the parameters and regulations that we have.
- What the law dictates
- Look at the safety of chemicals in dietary ingredients; level of safety
- We are well trained and equipped for safety reviews and evaluations of food substances and biotech plants (pesticide-resistant crops)
- Use the most conservative method (worst-case) of evaluating exposure, leading to higher safety.
- GRAS and Food Contact Substance programs have developed innovative notification programs responsive to the mission, with timely completion of tasks and reviews. Notices vs. petitions make them able to expedite work more quickly.
- Adequate background in accessing *in vivo* gene toxicology studies using all the information to identify the critical NOELs to use and to be able to use that information combined with appropriate safety factors to make an appropriate safety decision.

[REDACTED]:

- [REDACTED] has established industry guidance (Redbook 2000) and a standardized systematic review process for food additive petitions and other regulatory submissions. For a subset of these submissions, a primary reviewer (toxicologist) will request a pathology consult to answer specific questions regarding pathology-related data

[REDACTED]:

- On the regulatory side, we are pretty good at doing literature review, finding toxicity studies and summarizing them.

[REDACTED]:

- Follows the mission; always mission oriented.
- Applicability of existing methods to nanotech is a top priority under the Strategic Plan
- The program is looking at alternative assays: *in vitro* assays in response to an initiative started a few years ago called Toxicology in the 21<sup>st</sup> Century (TOX 21). This is something the Commissioner has committed the Agency to. With the idea of replacing the longer term, more expensive animal assay with short term, cell in a dish, type assays.
- One of the strengths of our research laboratory for chemical safety is our willingness and responsive to the needs of other Offices within CFSAN.

[REDACTED]:

- We respond to the issues we need to respond to efficiently, and generally as well as possible.

[REDACTED]:

- Neither [REDACTED] reviewer really listed a strength. Both commented on the lack of authority under the cosmetics mandates.

[REDACTED]:

- Using established procedure for evaluation and assessment of chemicals.

[REDACTED]:

- Do small chemical evaluations for food safety very well. We are getting better at stepping outside the guideline to make decisions. We get good support from research.
- We have standard regulations that are well established; use similar procedures and scientific approach
- Focus on this as our primary objective: To be sure chemical residue levels are at reasonably safe levels in food.

### Current with the science

[REDACTED]:

- We have state of the art chemistry knowledge & apply conservatisms to work around data gaps while maintaining protection of the consumer.

[REDACTED]:

- Recently: Increased focus on in-depth look at emerging issues, incorporating new methodology or considering whether it should be adopted. Work is done to the state of the science we are comfortable with.

████████: -The chemists and toxicologists are good at identifying deficiencies and corresponding with the notifier to either resolve the deficiencies or withdraw the notification.

████████: The █████ Process: participation in nominating compounds/chemicals for NTP conducted at █████: good collaboration between centers and transfer of information back to participants.

████████: -Constantly review the literature. Go to meetings when funds available, which allows us to anticipate potential problems.

-Have established a series of in vitro screening safety assessment assays, looking at anything from cytotoxicity to the functional assays that might be affected by an individual organ system: hepatotoxicity, neurotoxicity, kidney toxicity; trying to establish screening for cardiotoxicity.

-These four areas above have been identified by █████ as areas where research could assist in identification of components in supplements and botanicals

-Expanding spectrum to cover expertise and desires (before, they were limited to hepatotox): where we think the science is

Have potential to do and have done in the past some translational research with risk assessment elements

-Have found new ways to detect toxins (e.g., bacterial cell wall exacerbation); biologic and molecular research (not typical toxicology research, but important), emergency response (fast and dirty methods to extract a toxin: condensed for front-line responders; detect in a wide variety of foods).

-There is a critical need to develop reliable, sensitive, accurate, validated, fast, and economical methodologies for detection and qualification of nano materials to investigate health impacts or for risk assessment.

-Nanotechnology in foods and cosmetics is a new program. FDA is beginning to take a strategy to evaluate toxicity. There is not much literature available and so everyone is starting from scratch. FDA has formed strategy work groups and is slowly trickling down to our level in the laboratory.

-At our █████, we are particularly strong in reproductive toxicology and developmental toxicology. We are building our strengths in *in vitro* models for safety assessment. We have strength in nanotoxicology as well.

-Okay, *in vitro* models of the toxicology division; we cover (b) (5) █████ models. Scientists in other areas (*in vitro* neurotoxicology and *in vitro* renal toxicology) and other branches relevant to toxicology (nanotechnology) are doing well also.

████████: -Encouraged to keep up with new research developments.

████████: -We █████ have in some ways departed from the standard approach used by the Center for Veterinary Medicine for assessing the safety and effectiveness of small molecules and developed instead a hierarchical risk-based model that asks certain risk questions then looks at the best ways to answer those questions

## Quality of work

████████: -Very thorough reviews, scientifically sound, well documented, transparent  
-Conduct thorough reviews: take a deep look, discuss in teams (toxicologist, environmental scientist, consumer safety officer), then through division head before decision is made.  
-Staff with strong scientific backgrounds: perform thorough reviews, good technical documents; well received by other offices.

-We also discuss with the people doing the research as well and try to do some collaborative work. We do a good job trying to figure out what might be an issue. Then if there is something of concern we try to get some research done so we have our own in-house data as well.

-The review process is going well. It's a well-defined thorough process. The right expertise helps and is half the battle. The procedure itself is streamlined. There is a good sense of what goes after what and when. I think that the consultations for these voluntary programs are going very well. The companies or developers can talk to us at any point of their development.

████████: -The regular day-to-day assignments are well handled by the chemical safety review team.

████████ (████████):

-Conduct a lot of research with NTP and NCTR, including safety and exposure; cover as much ground as we can;

supplement with literature review.

-Research (█████ is meant to be the research arm of toxicology): what we do well is the animal work because that is what we have the capabilities for. Also the program is looking at alternative assays: *in vitro* assays in response to an initiative started a few years ago called Toxicology in the 21<sup>st</sup> Century (TOX 21). This is something the Commissioner has committed the Agency to. With the idea of replacing the longer term, more expensive animal assay with short term, cell in a dish, type assays.

█████:

-Research does a good job identifying issues after they happen and respond to issues at hand. Responsive to program office needs.

█████:

-Doing well but there is limited authority because no premarket approval. In the future, will need more authority. Mandated by Congress. Currently the project is working on safety testing guidelines. Europe is moving toward *in vitro* testing. Hopefully program moves faster.

█████:

-Diverse expertise. Can train people in specific areas (developmental or geno-toxicology). All areas of expertise can contribute to chemical assessments. Can get to the finer points of a review, while still maintaining a broad background overall.

-They squeeze the most out of the data that they have; impressive.

-What we do well is that we have consistent standards for each application. We try to be flexible where we can.

-For chemical safety reviews we have an established system and process and to some extent a thorough guidance base for reviewers.

-We hire really good people. Most of these people do not come with the exact skill sets or experience we need so we have to train them. They are probably “in training” mode for 2-5 years, learning what we do for residue chemistry. Because we haven’t been rushed into hiring, we can look at a pretty broad skill set and time to train them up to the reviews that we do. The program is good at integrating well-trained people and keeping them once they are in.

-Moving from a system that did not have that to the user fees we have been doing extremely well. We are meeting deadlines and producing high quality scientific reviews.

## Use of resources

█████:

-Do a good job with the resources we have.

Expertise of the scientists involved.

-FDA does a good job of getting people together with diverse knowledge for chemical safety review. █████ does a good job by listening to their concerns.

█████:

-The team is very consistent. Set guidelines that we follow consistently, but if we deviate to best fit a particular product, we do this consistently.

## Timeliness

█████:

-Timeliness. Able to be very fast for reviewing Food Contact and Secondary direct food substances. No regulatory hurdles to overcome and have kept adequate, if not ideal, staffing.

█████:

- We are timely within our mandates

█████:

Is able to address issues quickly; partly due to conducting acute vs. chronic studies.

█████:

-Risk assessments for recalls, import alerts, shortage analyses: all done quickly

-ADUFA deadlines, so we have well developed guidelines, templates, SOPs (internal) and P&Ps (policies and procedures, available on the web-site) to help us meet the deadlines.

## Data/info avail.

■:

- Obtaining and analyzing the available science via literature, all available sources they can find; not all of the data we would like to have are available.
- Not much. Redbook 2000: Although it is outdated and behind, it is the only mechanism to ensure compliance of chemical safety review with accepted science
- We are getting all the information needed to do our reviews. Have access to databases.

## Teamwork/Support

■:

- Good relationship between staff; collegial atmosphere.
- Working as teams, whether formal or ad hoc: chemist, toxicologist, environmental reviewer and sometimes a micro reviewer as needed. Hold regular meetings, so always aware of status of work in-house and what people need from each other (e.g., tox needs something from chemistry, etc.). Communicate well within the office and try to communicate with other offices but more challenging.
- Collegiality: chemists group meetings; still get together across divisions once a week
- The chemists are a very cohesive group
- Personnel: strong, diverse backgrounds; cross support.
- Can ask for help within the division or from other chemists outside the division
- Collegiality: chemists group meetings; still get together across divisions once a week
- Chemists work well together; meet weekly so the way they do exposure estimates is cohesive.
- Good team, good collaboration among chemists and we also collaborate with the rest of the review team, toxicologists and consumer safety officers (CSOs).

As a chemist, we do a good job talking among other chemists in our office. We also discuss with the people doing the research as well and try to do some collaborative work. We do a good job trying to figure out what might be an issue. Then if there is something of concern we try to get some research done so we have our own in-house data as well.

■:

- Strength of the review process is that it is an interdisciplinary approach that works very well. There is a chemistry angle and a toxicology angle. We have a wide variety of expertise that feed into the review process.

■:

- They do well in getting the appropriate scientific expertise. There is a variety of backgrounds, but collaboratively they cover all aspects of the issues that come up in our Office of food additives.

■:

- Work well as a team and with other teams and divisions; this is important for novel products
- Collaborate well as a team/division. Can consult with each other. Everyone is open and willing to help out with problems that come up with a review.
- Diverse backgrounds: 3 teams doing human food safety assessment, each specialized in a different area: toxicology focuses on hazard identification and characterization, res chem on exposure assessment and mitigation, and microbial food safety on antimicrobial resistance and effects of antimicrobial on human gut flora. The 3 teams have to work together.
- The mentorship from team leader is highly regarded; she is very experienced, works very hard, and is devoted to her job.

## Other

■:

- Providing guidance/consultation to industry in pre-petition consultation, concerning what kinds of data are needed to make the safety decision.

■:

- Work well with industry; try to have a good relationship with all of our stakeholders



## 2. What do you see as the most obvious weakness in your program with respect to chemical safety review or research?

### Feedback/support

[REDACTED]:  
Lack of regular and consistent communication between reviewers and research scientists: frequent/regular/issue specific discussions, bringing in research scientists early on would enhance both.  
- Although things are generally improving, there is a lack of support (money and training) from management.  
-From a research standpoint it is hard to get feedback from program offices to find out about what kind of research they need. Better dialogue needed between the program offices. Involved with [REDACTED] and Cosmetics but no interaction with Chemical Hazard Assessment and Exposure Assessment Teams. Better involvement to make better informed risk assessment decisions. Chemical Assessment Team is a piece off on its own. Better integrated with toxicologists in the research area and [REDACTED].  
-The reason brought on as the [REDACTED], was the recognition that the toxicology program was under-funded and under-supported for many years, and needed to be built up. That is where the weaknesses are: under-funded, under-supported, and under-manned. Also, communication between the Offices is a problem that we are working on as well.

### Peer review

[REDACTED]:  
-In the immediate program (food additive and ingredient safety) need to modify procedures to include more internal expert committees.  
Because the nature of the evaluation is subjective, toxic endpoints may be interpreted differently. E.g., for animals vs. humans, there may be differences in what is considered significant, insignificant. A possible solution to this is to have multiple levels of QA so that we can compromise or reach an agreement.  
Scientists (toxicologists) should discuss with other toxicologist to make my point if a chemical is safe or not. But in some cases the administration (with no background in toxicology) is giving direction to the scientists.  
-Cultural view of toxicologists - told by senior management that anyone can be a toxicologist. In some divisions that view has translated into an interference with safety assessment. Preconceived views of upper management that the underlying hierarchy is that toxicologists are the “lowest man on the totem pole”. View of upper management that chemistry is real science.

[REDACTED]:  
Need wider peer review of their decisions coming out.

### SOPs/procedures

[REDACTED]:  
There has been a pronounced decrease in emphasis on review to the detriment of the risk assessment practices we use. There was formerly a better balance of chemical and microbiological safety assessments. More attention to how research was done for e.g., carcinogenicity assessment.  
-Hands are tied for prior-sanctioned compounds, old dietary ingredients. For new compounds, once they give us all the information, we have to let them use it.  
[REDACTED]:  
-There is a lack of broad toxicological knowledge, failure to incorporate biochemical mechanism and modern *in vitro* technologies into new toxicological studies and Agency reviews.  
[REDACTED]:  
-There are no set guidelines for safety review. There are no SOPs on how chemical safety reviews should be done. The 2<sup>nd</sup> tier of management research funded by the Office should be tied into regulation. What are the goals? A system should be set up.  
[REDACTED]:  
-We are not proactive enough in anticipating new issues that could be coming on. We don't use historical data well in terms of trying to present an overall picture of where the hazards are and when they come up. We are really in a case-by-case basis and we could do develop a more comprehensive approach in terms of how do we maintain our data and know what we said in the past so that we are consistent, and establishing proper procedures for making

decisions based on as the hazards come up.

## Manpower

[REDACTED]:  
-Industrial chemistry is not as well covered. The program is always short-handed. Sometimes rather than rush to a conclusion, if there's a problem, we have to reject. If there were more time we might not have to do this, could do some additional work to move something through that might otherwise have been tossed out.

- A redistribution of workload may be needed.

-As we lose people we are losing their institutional memory and also losing time for documenting and writing good memos

-It is a voluntary program and so one of the aspects is that we don't know how many submissions per day we will receive and so the resources are stretched

[REDACTED]:

Really don't have enough manpower for the work.

-Extra projects (e.g., where the real progress in risk assessment occurs) get pushed to the side.

-Organizational structure is weak. The safety reviewer's group (toxicology/pathology) is small and scattered. The scientific base in the entire office has eroded.

-Could use more staffing in research and review (especially Office of Chief Counsel) to improve timeliness and coordinate jurisdictions.

-When I joined the staff, there were about 20 toxicologists, now the staff has been reduced to around 6 people.

Scientists (toxicologists) should discuss with other toxicologists to make my point if a chemical is safe or not. But in some cases the administration (with no background in toxicology) is giving direction to the scientists.

-We have limited resources and a large number of submissions, a lot of tasks for the day-to-day assignments. Therefore we do not have enough resources for special projects.

[REDACTED]:

There doesn't seem to be a good plan for replacing staff that leaves/retires: How do you find qualified people to replace experienced staff.

[REDACTED]:

-We don't do well with respect to research. The reason for that is in the early 90s we had a [REDACTED] that despised the [REDACTED]. When he had the chance he did everything could to try and close down the program. The culture has since changed. Now they seem to be trying to reinvest in the toxicology program. But they have almost no one left.

[REDACTED]:

-Lack of resources to the program because there are so many possible issues. Cosmetics is a lower priority on a lot of people's radar; therefore, the resources and authority we have to deal with these issues are limited.

[REDACTED]:

-There is a big gap in age and expertise. There are people with 30+ years experience who are leaving/have left and cannot be replaced or back-filled

-Lack of foresight to hire to replace people who are leaving, resulting in a loss of experience. Hiring the right people is difficult. Doesn't need to be a permanent hire. Can do "directed hiring"; contract Fellows for a defined project, but this is short-term.

-Because we are under-funded and under-manned it is difficult to remain state of the art science.

[REDACTED]:

-There are dwindling resources; there used to be twice as many toxicologists as we have now.

-Our group is greatly understaffed. The people carry a very heavy load. They don't fill-in after retirements. Because of the workload there is no time to keep up on areas we are experts in.

[REDACTED]:

-Lack of resources for enforcement, inspection of overseas facilities. Could be taken advantage of.

-Resources: get work from many different sources. Sometimes don't have time/money to stay current or go to meetings. May not have money to have the appropriate staff that we need to appropriately cover everything.

-May not have all the specialized expertise needed; may need outside help on pathology and immunology. The team has lost a lot of senior expertise, and has a lot of new team members who need to be trained.

-We are short of people. Too many side projects besides our review work. Also too much administrative work to do.

The weakness in the program is getting and keeping the right people.

-The natural turnover of people when they retire or move to a higher position.

## Timeliness

■: -Direct Food Additives program hasn't changed in a long time. The lack of timeliness of FA petitions creates a bias in the industry to prefer one program (e.g., GRAS) over the other if a substance might qualify for either.

Industry wants predictability. Could improve their perception of the DFA program if they had an idea of how long it might take.

■: -Regulatory procedures make things slow and cumbersome: time commitment and redoing reviews, a lot of back-and-forth with time lag. Can be inefficient. Can be frustrating, especially for new substances. We're not the only agency with jurisdiction over certain compounds: overlap with USDA and EPA can affect the regulatory process, that don't have much to do with the chemical safety review per se.

## Data/info avail.

■: Difficult to get all of the data we need from industry (confidentiality issues?); they are not as forthcoming as they could be

-Using assumptions (worst-case) based on stated intended use or use conditions to cover uncertainty; these assumptions and scenarios may not reflect the actual situation.

-Since we do not do research, we are limited by the amount of information that industry provides (won't provide if not mandatory) and the amount available in the literature. As a result, need to make decisions based on limited information.

-A variety of data sources that we have been getting a hold of by contracting but this year we have "x" number of dollars to spend, we can buy that piece of software now but the markets are changing with respect the type of food packaging that are being used, new ones come on the market, and the old ones disappear. So you have to have some type of steady state process to keep that information up to date

■: -An apparent legal or technical weakness is the legal aspect of GRAS, in that it is a voluntary program with no legal authority to ask for more information. But in reality, they talk with the companies, talk science, and put them in the position of voluntarily complying. Therefore, the restriction is not a practical weakness. Believes the safety standard is maintained.

-No interest in advancing/accepting new knowledge; hesitant to accept new approaches to analyzing data without validation. Management hesitant to try new approaches or consider new information (e.g., there was concern about BPA decades ago; for trans fats, should consider new information, even if it's not consistent with what's out there.

-Lack of data: rely on industry; therefore, may see only one side of the story. There is a lack of balance

-There have been advances in science that haven't been incorporated into animal testing: no pharmacokinetic data are requested. Some controversies could be avoided if we had additional supplementary research information: EPA has this.

-Now have to deal with what is submitted. Very hard to ask for more data (ask them to explain, but not to redo). Think we used to ask for more. When we raised issues based on science, it seemed that industry responded in kind. Has heard that DFA petition process will be replaced by a GRAS process. This would be bad for the consumer. No matter how good your scientific argument is, it is inferior to "something" else that is driving the whole process. If the science and characterization are published and clear from the beginning, addressing all issues, we can head off skepticism. Need to do more work to defend the science decision and protect the company who registers the product--we say it is safe, not them.

-Have not addressed new trends like in vitro testing. Not convinced that we should rely on this (will provide additional insights). May not be a sufficient surrogate for what happens in the intact animal--especially for metabolism and pharmacokinetics.

-Congress doesn't view FDA as having an important role in research breakthroughs. Research is not funded like it is for NIH or DOE. There are questions that could be answered more expeditiously by our own scientific staff, rather than contracting the work out.

-Sometimes we don't know if the amount of chemical they say is in a product is accurate because we don't actually

go out and test it and have no way to test it.

-What we do is limited by the law and the regulatory environment. GRAS is a voluntary program; therefore, may not always be notified of all substances (no premarket approval), and they may "sneak" into the food supply by self-affirmation. Therefore, we cannot play a greater role in the kind of data to be developed.

-We lack a complete market survey of available products, and when we ask for information, there are delays.

-We do not have actual cumulative exposure information from all sources. We are very good at assessing exposure based on the intended use or the uses we're aware of. But in terms of uses of something that is regulated by EPA, we don't have real cumulative exposure.

-Don't have complete data packages; database, information is incomplete and therefore decisions are based on own interpretation. Never get complete information like CDER (drugs).

████████: (b) (5)

There is no database for chemical safety. This would help to identify toxics, especially for combined or multiple ingredient products.

████████:

-Our safety standard in our current toxicology guidance states that we should use the cumulative exposure for the chemicals in order to decide if there are adequate toxicology data. However, in practice, this is very difficult for the chemist to calculate a cumulative exposure

████████:

-Nanotechnology is such a new program there is a lack of experimental data to make a risk assessment of these particles. Waiting for more experimental data to become available for safety assessment.

████████:

Lack of consistency in the way we do assessments, the way we ask for data. No consistency in what data are to be used in a given situation. Lack of record-keeping. There is not a good way to go back and look at previous issues.

████████:

-We could do more research in infant and child safety (the 10x safety factor may not protect for new chemicals and proteins, diseases and allergens)

-Could use better methods: animal tests don't detect new chemicals including proteins, and allergens aren't covered by the traditional approach.

████████:

-Research does not support classic toxicology (rats, mice, dogs, rabbits animal testing) and we do not provide support for safety to the human gut flora (effect of residue in food on human micro-flora in the GI tract)

-Difficult to stay current (training, conferences, meetings) due to insufficient training/meetings (limited by budget)

-Same with research-confined to budget so many things are outdated.

-Need to adhere to specific mandates so difficult to stay with new developments--these tend to get back-burnered

-Maybe not a weakness, but we often struggle to accept (b) (5) -usually because we are not privy to the primary data. -It would be helpful to have access to the data so that we could decide to accept or come to a different conclusion. Now there is no such mechanism: we need to check published information instead to make our decision as to whether to accept or not.

-Basic aspects are covered well, but would like to see better data. Sometimes the data are not that great for making a good scientific decision; therefore, we sometimes need to make assumptions/judgments that may not work to the sponsors' advantage.

## Communication

████████:

-Lack of willingness to reach across agencies more aggressively for data. All agencies should have access to CBI.

████████:

-Lack of regular and consistent communication between reviewers and research scientists. Before everyone was together, now they are separated.

-Issues and questions do not come down the chain of command. Relationship between research and the regulatory office needs to be improved. The questions do not come down to the research level.

████████:

Lack of communication with other groups. Sometimes we may not know who else in the Center has similar expertise.

[REDACTED]:

- -Have been against publishing: we sit on a lot of good data; could do better getting that out to the public.
- Our reluctance to publish does not help us.

[REDACTED]:

- We are a consulting division for other divisions: sometimes communication across division isn't great.
- Sometimes each team wants to do their own thing (don't touch our part), but really need to work together. Need to understand all areas. Sometimes they communicate but don't want to change their area.
- The problem is the integration of our part with other Centers. In my view there is only one human health, basically we humans are exposed to chemicals from a lot of sources. Chemical exposures from CFSAN (food from supermarket), CVM (residues chemistry -- food producing animals), and EPA (pesticides). It is the integration part. How much human exposure for all these sources? Example: Acceptable daily intake (ADI) from different places but there is only one human taking it all in. There needs to be some kind of coordination between Agencies. Determination of the cumulative effect using one number. Right now each Agency involves gives a separate number.

## Not Safety

[REDACTED]:

- Because it is a voluntary program, we are trusting the system will take care of the safety. We are trusting that developers will come to us and talk to us. Don't know if that is a weakness but there is always someone looking for a loop-hole.
- Using assumptions (worst-case) based on stated intended use or use conditions to cover uncertainty; these assumptions and scenarios may not reflect the actual situation.

[REDACTED]:

- 1. Inability to know whether we're wrong/causing harm; difficult to tell because of lack of confirmatory information.
- Need more market testing to check levels of components in food: real-world experiments to detect/confirm that we are not doing harm and that we're meeting our goal of low/minimum levels of exposure.
- 2. Our approach might not be right for:
  - Mixtures. We do not address even closely related components
  - Exposure calculations. We use average exposures/consumers, but do not consider those self-selecting their diets (mega-doses of vitamins, susceptible populations, etc). Might be useful to look at 90<sup>th</sup> or 95<sup>th</sup> percentile, then use a Bayesian or probabilistic approach to determine exposure.
- When called on to do work outside the law (e.g., post-market work) need more money, staff
- 1. First, the inability to understand the difference between risk assessment (best estimate of risk to humans with the data you have) and risk management (what you do about it to reduce risk in consideration of cost, approach, law politics). As a consequence, risk managers want risk assessment to fit their agenda; risk assessors are worried that risk manager's will "slight" their risk. These have been lumped in the past, but need away of keeping the two from influencing each other.
- 2. Second, the inability to come to grips with dose response characteristics for toxicology limits the ability to characterize the risk. The approach to chemical safety has been outdated for a long time.
- Concerned about the safety of the products that are approved (mission), but understands that the Agency needs to do good work for the sponsor/petitioner. In some areas they could do more safety screening before submitting, but not all. Now we try to provide the best option for the sponsor to get a product to market. This means we do not necessarily deal with all of the science issues that pop up. Responsible petitioners would want solid science in support of their product.
- Some ingredients may get through but the information is not publicly available, and there is not always a consensus of safety, mainly because industry keeps proprietary. This is beyond the control of the group.
- Cultural view of toxicologists - told by senior management that anyone can be a toxicologist. In some divisions that view has translated into an interference with safety assessment. Preconceived views of upper management that the underlying hierarchy is that toxicologists are the "lowest man on the totem pole". View of upper management that chemistry is real science.
- Our conservative approach to food safety or assessing the safety of food additives is also a weakness in a way because the safety factors that we rely on when doing a safety assessment were developed in the early to mid 50's. They are based on the science and policy of that day. Since then they really have not been changed. We have not

tried to make our safety factor approach current with science.

-Dietary exposure assessment: this is the most accurate of any of the parameters that go into a risk assessment. The rest of the risk assessment factors are in need of re-assessment. Yet, the segregation of the exposure assessment from the toxicology dose-response assessment and the risk characterization of integrating both of these to estimate the risk, or safe dose, are not done collaboratively. Do the estimates well, but there is difficulty in assessing the impact.

[REDACTED]:

-The main problem would be that we have to meet unreasonable expectations in terms of meeting safety standards that cannot possibly be met. It's largely because there are different standards for different programs and you can't apply the same standard all the time (e.g., you cannot apply the same standard for contaminants as food additive [REDACTED]):

-Not certain risk assessment has all the data they need. Our stumbling blocks and challenges are the authority we have which Congress gives us through law. Federal Information Security Management Act (FISMA) has opened up a lot of doors and they working hard on getting those initiatives fulfilled but we still have considerable gaps. Don't see the linkage being done. If it is being done by management then don't feel it's being fully articulated in a way this is getting at. Risk assessments have been done that don't address the public health issue, the vulnerable population. Having direct linkages and saying here is a list of public health issues and underlying that these are the data gaps, this is the research, and this is the risk assessment. (b) (5) [REDACTED]

[REDACTED]:

-Lack of resources for enforcement, inspection of overseas facilities. Could be taken advantage of.

-Resources: get work from many different sources. Sometimes don't have time/money to stay current or go to meetings. May not have money to have the appropriate staff that we need to appropriately cover everything.

-- Things are more focused within the offices because of user fees--has resulted in a dramatic change. We are now dealing with a paying customer can lose sight of the fact that we are tasked with finding safe and effective products. There is a different viewpoint on getting something approved vs. whether it's safe. Also, submission quality has gone down, even though we are giving them more recommendations. There is not even time to read a scientific article, unless for a specific focus group or team. No time for us to look for developing trends, instead they tell us what the trends are going to be.

-One of the things I don't like about our program is the people that do that, mostly veterinarians and animal scientists, have a vested interest in getting a product approved and fully appreciate the value. We are often pressured to move our review along, move our safety and exposure assessments along. Because the longer we take the longer before this product is out there.

## Post-Market

[REDACTED]:

Can get over-burdened with work. Now there are more post-market issues that need to be addressed & office is not really designed for that. Tough to balance between new issues and established workload, and deliver a quality product on time. Resources (personnel) are stretched to the limit. Other resources seem to be adequate.

[REDACTED]:

-We are fighting to keep up with the post-market review side. We have to stress staff resources from the pre-market to address questions for post-market reviews

-When called on to do work outside the law (e.g., post-market work) need more money, staff

[REDACTED]:

-(1) Changing [the standard] routine or dealing with things which don't fit into the routine or the standard paradigm of [safety review]. (2) Once a decision has been made there is no mechanism to go back and revisit it later or update the results.

[REDACTED]:

-Don't have a re-evaluation program for things that have been approved (e.g. 5 or 10-year re-evaluation to see if the scientific evaluation has held).

## Other

-Funding mentioned by 3-5  
-We are reactive instead of proactive.  
-We are losing our edge in some respects; seem to be falling behind EFSA (who are more a scientific body than scientific and regulatory).  
-We only review something when we are petitioned; they tend to go out and take action.  
-Could do more evaluation of emerging technologies--take a better look at how they would benefit the program.

████████:  
-It would be nicer if training money were more accessible.  
-If results don't conform to a given concept, others assume they are incorrect and that the group is not "doing it right".

████████:  
-Management hesitant to try new approaches or consider new information  
-Being asked to follow up on ideas that are outside of the mission; try to go beyond what we are asked to do. We tend to get caught up and utilize resources that are better used elsewhere  
-There is no regard for training, background, or any expertise. Our supervisors do not go through peer review. Just because you take on the mantle and responsibility of supervising people does not mean you have the expertise or experience to lead, or desire to understand where our needs are in terms of public health.

████████:  
-Young people come in and they usually have state of the art education or whatever their specialty is. There is no emphasis for them to broaden their knowledge particularly to learn modern toxicology. There is no encouragement for anyone to go back to school or the lab to enhance skills you came in with.

████████:  
-Clarification and expansion of the research role of █████ vs. NCTR.  
-My program and the entire Center has significant leadership problems. The science is not lead well, not on a Center level, not on an Office level, not on a Division level.

████████:  
-Was hired full time to help with the mathematics, statistics, and programming that is needed both to do the calculations we need and to understand when people come to us with data, what they did and to be able to translate it in a sense. There isn't really anyone else in the Office with an engineering or mathematical background. The chemists are very smart with what they do, but they don't have that mathematical expertise and are expected to do that piece. It would be optimal if they had more people with mathematical backgrounds. It's hard because they can't just hire anyone. For the Office it says to hire chemists for chemistry reviews, even though there is more than just the chemistry piece that goes into a safety assessment, chemistry-wise. (b) (5)

████████:  
-No work is being done on public health issues that fall under a broader category: No strong translational or risk assessment research is currently being done: No one is assessing how toxins are affecting overall human health (e.g., complicating effects of any agent on susceptible populations, Alzheimers, cardio). Bacterial toxins are totally ignored with respect to risk assessment, yet these can lead to respiratory allergies, colitis. No work being done on allergens, structural analysis, molecular analysis of how nutrients act (vitamins), genetic regulation of aging, obesity, food products as medicines, rapid detection methods for chemical contaminants (plant or bacterial).  
-Fluctuations in funding  
-In my Division I do (b) (6) █████, but think that intestinal absorption is related and needs to be emphasized s).

████████:  
-We are resistant to change, but the climate is changing  
-Have been against publishing: we sit on a lot of good data; could do better getting that out to the public.  
-Our reluctance to publish does not help us.

████████:  
-Timidness to make decisions: it seems to be a long process to get to a final decision (maybe not the "right people in the room"), even given the scrutiny under which the Agency operates.  
-We may get pressure to approve a product on behalf of another division ("can't you do it this way?")  
-One of the things I don't like about our program is the people that move applications through the system, mostly

veterinarians and animal scientists, have a vested interest in getting a product approved and fully appreciate the value. What spins out of this is on the residue chemistry end is that we are often pressured to move our review along, move our safety and exposure assessments along. Because the longer we take the longer before this product is out there.

**3a. Are you aware if chemical safety risk assessment and safety evaluation methods are consistent across offices and centers?**

[REDACTED]:

- There are differences at the policy level across offices. Petition review for DFAs, but similar products can go through GRAS without data submission or rigorous reviews. Food contact notification program has many different options for a product to get to market without a thorough safety evaluation.
- CDER chemistry is similar to CFSAN in approach but different in focus, but they are more focused on the manufacturing process and impurities. In Foods they are more interested in the general purity of batches of products. Where needed there is good interaction. Fundamental review is the same. Different focus on safety.
- On the review side of things, there is little interaction across Centers and Offices within CFSAN and so cannot speak to the specifics of risk assessments and whether they are consistent across Offices and Centers. Within Office methods are consistent; the chemists have weekly group meetings to discuss problems and that they are on the same page. The toxicologists and CSOs do that as well. They may need to be encouraged to do it more often.
- Within our Office it is definitely consistent. Chemists meet every week to discuss issues that are coming up with our reviews. There is a lot of interchange of help. We use similar programs as well, software analysis tools. Within the Center, does not know. Would assume the labs have similar risk assessments. We do collaborate on some topics.
- We do biotechnology reviews and work actively with [REDACTED] scientist experts. We are looking at human safety and they are looking at animal safety. Very different requirements.

[REDACTED]:

- Do not think that CFSAN and CVM have significant differences in data submission and data interpretation that cannot be justified by differences in the regulatory mandate. CDER is different due to emphasis on human data
- The principles are the same and ascribed to across all programs.
- Never happens across Offices and Centers because of proprietary information, trade secrets, regulatory routes limit information sharing.
- Yes it is consistent because we do the carcinogenic chemicals and risk analysis. We have a standard procedure that we follow. It is required, mandated.
- The structuring for all of these [Offices, including [REDACTED], [REDACTED], [REDACTED]] is very different.

[REDACTED] ( [REDACTED]):

Don't know. There is no communication between centers.

Yes. Consistent on the whole, but different because there are different substances (drugs vs. contaminants). All use established scientific methods to come to safety determinations.

[REDACTED]

- Vs. other Centers, assessment and safety evaluation methods are consistent in practice and are consistent with the accepted regulatory processes of risk assessment.

[REDACTED]:

- Similarities between CFSAN and CVM vs. CDRS re: data requirements.
- They are not consistent but there are many scientific reasons for that. It would be advantageous if :
  - (a) The Offices and Centers were aware of how everybody does do their reviews and there was a knowledge of it; and
  - (b) there would be an attempt to streamline it as much as possible. There is nothing wrong with a good old standard operating procedure (SOP). If we had an SOP thinks it would be more streamlined and easier for those to understand that come from the outside.

[REDACTED]:

Not a lot of consistency across the offices. There are different evaluation methods for different offices (e.g. CFSAN vs. CDER) due to differences in regulatory authority and requirements for each office for chemical safety evaluations. Not a lot of cross-talk, several methods.

- Differ across Centers because of the different statutory mandates.
- Aware that chemical safety risk assessment methods for all Centers including NCTR are consistent; however, not sure for safety evaluation methods that all the Centers are on the same page because it is a new program.
- That is difficult because not aware of other Offices and Centers, don't know what they are using for safety risk assessment. That is something that should be covered better.

[REDACTED]:

For contaminants, we generally work with publicly available data. There is no pre-market approval, there is no

standardized submission, and there is no registrant. So this question does not apply. There are some cases we could discuss the underlying science and get to some consistent resolution. But we don't, we generally don't talk to each other. In case of inconsistencies, communication would help. We tend to work on different chemicals and so it is not a huge issue, but in the case of arsenic we were all working on it and did not talk.

████████:

Methods are not consistent. Each office has its own issues. Some believe theirs is the only way to do an assessment.

████████:

-Different offices have different regulations. Between █████ and █████, they try to be consistent but there are some gaps.

-An externally applied cosmetics has a very different risk profile than does an ingested dietary supplement (e.g., like ephedrine which has a cardiac stimulating effect). So while there are some similar areas so you can characterize an ingredient or product and have some standard characterizations (like high, medium, or low risk), the approaches need to be tailored to product and it's level of actual risk.

████████:

-The regulatory mandates and therefore the programs and assessments have to differ to meet those mandates. There are clear differences and there should be for what we can/should ask for a GRAS application vs. a new animal drug application vs. a food additive petition.

-Methods of evaluation may be very different, but trying to standardize the overall evaluation with slightly different endpoints. CVM's GRAS Notification process is modeled on CFSAN, but not copied exactly because of the manner of exposure.

-Centers: not sure. Offices: some differences depending on the type of drug or compounds. Within the division it is consistent across 3 teams in how we review assignments. For other offices, they may try to get things out quickly and not take a hard look at the assignment.

Risk assessment approach is generally consistent, but there is different emphasis. Depends on the product.

-There is a different emphasis for human food safety vs. drug safety. Different populations exposed, different risk/benefit considerations. This leads to different review-based considerations.

-One of the weaknesses for the Office of Food is that we really don't have much knowledge of what each other does in the two separate Centers.

-They are reasonably consistent and the differences are understandable. CFSAN harmonizes more through OECD with EPA and we harmonize more through VICH. But we are aware of each other's. The safety standard is identical for pre-market approval: reasonable certainty of no harm. There is international support for those safety standards in both. We both rely on Joint FAO/WHO Expert Committee on Food Additives (JECFA). There is a JECFA for human food additives and a JECFA for residues of animal drugs.

-For pre-approval for a new animal drug we see raw data. We are trying to be a lot more open to alternative approaches within the limitations of the law. Can look at summary reviews and can decide what is the most and least important. Don't know that this happens universally across the Agency. In CVM, pre-approval ONADE we have a wonderful opportunity called "phased review". Phased review allows us to see little bits and pieces without seeing the whole package all at once. We are able to focus on the study, we can give the sponsor very focused comments, and it means that the whole operation doesn't fail every time it comes in. It seems that other parts of FDA and part of CVM too that interacting with sponsors is not encouraged.

████████:

-Don't think there is consistency because there are slightly different missions; the data requirements are different by law almost. For example █████ has certain requirements for human food safety evaluation of new animal drug applications, while what we do in animal feeds is slightly different (looking at feed petitions). There is a lot of overlap but a lot could be done in maintaining consistency. We could do a much better job at being consistent. We certainly try when possible but think it could be a higher priority for the Center.

████████:

-Not concerned about whether or not a specific methodology differs slightly from one Office or Group to another; instead about whether or not the characterization of the hazard, the determination of the risk, and the findings of safety are done with the appropriate level of rigor.

### 3b. For example, are there consistent requirements for submission of raw data and data tables?

- The requirements depend on the law. For direct FAs, there is a regulation issued. GRAS notifications just look at and assess what is done outside. Like to think that they are the same safety requirements, and hopefully that's true.
- Within the office, there are different requirements for data between food additive petitions (raw data) vs. GRAS (summary of available data and some submitted data).

[REDACTED]:

Within the office, different divisions - using the same concepts, programs, procedures for making dietary intake estimates. No differences for these estimates because they use the same software, same input

- There are differences in actual risk assessment practices across centers (between CFSAN and CDER). CDER and ENEA and Japan worked together to develop harmonized guidelines (ICH; International Conference of Harmonization). They have a guideline for harmonization of immunotoxicity data. But CFSAN does not have an updated immunotox guideline in the Redbook. It just has a link to the 1993 draft (which is close to the CDER guideline), but CFSAN does not currently use this guideline. In a certain review, the data indicated potential immunotoxicological concern. If you followed the ICH guideline, the petitioner would have had to address this issue, but using the current CFSAN guidance, no additional data were required.

-Consistent within the division but not across centers. For example, has not seen any CVM packages or even different divisions within her own center, so not sure they are asking for the same things.

[REDACTED]:

-CDER, CBER and CDRH put much less emphasis on toxicology studies in laboratory animals because they usually have human trials or data, which CFSAN and CVM usually do not have; different data available.

-For chemistry, we are consistent. There are guidelines that have been set out by the chemistry review team for the types of data they want to see. Although it may not always be in the same format from one submission to the next, we are getting the data. If you're not getting the data you may ask them for it. There are no standards but they are working on this at FDA (electronic formats for clinical and non-clinical data to be submitted).

-There is a certain inconsistency across the Center about what types of information they do receive. It often depends on their regulatory purview, if they have a pre-clinical approach or don't have an approach. Example: Our dietary supplements and GRAS groups just see summaries of the data that comes in and our cosmetics group may not see anything at all. There are some assumptions that somehow the manufacturers are ensuring that cosmetics are safe.

[REDACTED]:

-Different research is being done across offices and centers. There are different ways of approving projects and different requirements for data presentation.

-That is totally consistent. Encompassed under Good Laboratory Practices (GLPs). That is pretty much uniform across the Center and across Federal Agencies as well. All human safety data are required to comply with those GLP regulations.

[REDACTED]:

-There are consistent requirements, the inconsistencies are usually based on exposure levels or differences in the purpose of what is submitted.

[REDACTED]:

-For genetic toxicology data a previous supervisor said, "If we want to have internationally accepted guidance, we, as individual employees, need to form a working group, and agree on this stuff. If we have people from all the Center in this group management would accept it." And that is basically what happened. The subject's expertise is pharmacokinetics and is considered the Center expert on pharmacokinetics. Has talked with his colleagues at CVM and CDER and we've tried to come up with consistencies.

[REDACTED]:

-Our Office has a very defined website which outlines what kind of data we are expecting. However, because each compound has its own intricacies we recommend a meeting with industry before they submit so we can give them some sort of feedback about what kind of data we would suggest based on the situation they are painting.

[REDACTED]:

Many premarket review programs lay out information requirements in guidance and are authorized to require that submitted lab data be collected under GLPs. Programs that rely on historical use (e.g. GRAS and NDIs) have a very different paradigm and must frequently rely on non-GLP data which may be published in journals or not. On the other hand, [REDACTED] does seem to be starting to explore dose-response risk assessment, but does not appear to be doing so in collaboration with other risk assessment groups in the Center.

[REDACTED]:

Should begin looking at other kinds of data.

-There should be a standard approach, but this should not be the only evidence considered

[REDACTED]:

-Although the format of the submissions is flexible, they are consistent in that GLP is required. It is difficult to interpret if something that has been performed under GLP-like conditions can overcome the lack of GLP.

Sometimes use weight of evidence approach, using published literature to support a given study. Sometimes this is not consistent.

-For vet drugs, you may have different sponsors, small companies who can't afford large studies; therefore, you need to find other ways for them to fulfill the data requirements (e.g., use of published literature, rather than raw data). Rather than a large study, they may only need to do a small portion of the study to fulfill the requirements. It seems that small companies, new to the process, may get off a little easier. If they're new to the process, we may hold their hand a little more or let them bypass some steps, but we will never pass anything that isn't safe and effective.

-The general risk assessment principle is the same, but found it was different than CFSAN when doing a peer review.

-The data requirements are reasonably consistent for pre-market. The post-market people have to rely on what is available in the research already and so there are no requirements *per se*.

[REDACTED] | [REDACTED]:

-What is required for raw data and data tables is very spelled out for new animal drugs stuff. It is not as clearly defined for animal feed petitions. This is across the Center [CVM]. Across the Centers [CFSAN and CVM] we could do a lot better job. But again, part of it is different missions. They are looking at something different.

### 3c. And if not what is the rationale for the inconsistency or inconsistencies?

Where there are differences, they are based on regulations, guidance, and standards, set up over time for their office/programs

\_\_\_\_\_:

-There are some inconsistencies, but they conform to laws and regulations. More stringent requirements for some types of chemicals than others: carcinogens fall under the Delaney Clause; therefore, a food additive is out, but an impurity in the food additive may be OK, regardless of whether the safety data are adequate to support the food additive itself.

-There is no clear mandate, such as aligning to the strategic goals of FDA. Specific goals for review work could be defined within the division (minimum safety/competency from industry). There could be an external look at the different types of reviews (something like the Pugh review, but with more familiarity with the work and a proper background) to assess whether they meet minimum standards and improve internal standardization.

-The inconsistencies can be based on a reviewer and their level of experience. It can be based on the seriousness of the issue. It could be based on how people interpret the data. From the GRAS program we expect to look at summary data and the data is supposed to be publicly available, all the raw data should be in a publication already. When we see raw data it is usually a flag for us that these data have not been made public, unless it's raw data in a public report.

(b) (5) scientists look at the statistical side of the raw data whereas (b) (5) scientists look more into the meaning of the data.

\_\_\_\_\_:

-As mandated. As available in peer reviewed journals. The data are assumed acceptable. Questions should have been addressed at peer review or rebuttal in alternate publications. However, we don't just accept what is provided, but also look for ourselves.

-Requirements for submissions vary-what aspects and how they are looked into. For GRAS, don't need raw data, but for food additives petition review do see raw data. Our review is based mainly on the toxicology studies; unpublished data that are used are corroborative. Also, vs. CDER: we look at safety, they look at risks/benefits.

- There are some inconsistencies, but they conform to laws and regulations.

-More stringent requirements for some types of chemicals than others: carcinogens fall under the Delaney Clause; therefore, a food additive is out, but an impurity in the food additive may be OK, regardless of whether the safety data are adequate to support the food additive itself.

-Differences in different centers due to different products. For CVM, animal products must be tested for different sensitivities in different animals; therefore, need a broad scope. CFSAN chooses animals that are similar to humans (mouse, rabbit, dog, rat).

-The rationale is that not every study is equally important; however, where raw data are not available they can be requested. Production of the data is time-consuming and may not always be of value.

Some are justifiable: Some studies merit more consideration than others. Safety questions and issues should drive the merit of the study

-Each Center is unique. CFSAN has more willingness to share data, but other Centers do not.

-It depends on the regulatory paradigm they follow and how Congress has seen fit to give us regulatory authority. With the ICH approach there is a harmonization effort because drug regulation by necessity has to be universal. The other part is what kind of regulatory authority do we have? Our dietary supplements group has very little, as does our cosmetics group. They don't get a whole lot of information regarding the safety of these products. The Division of petition review probably receives the most information within the Center because we are looking at direct food and color additives.

-For different products, there is an assessment of degree of rigor or the data needed or the degree of concern regarding the product safety. Therefore, indirect additives get less data than direct additives because you are ingesting the direct additives.

\_\_\_\_\_:

-Groups differ on the type and amount of safety/tox information required and conservatisms employed, but the final evaluations and conclusions will be consistent.

\_\_\_\_\_:

-Within the Office it is consistent. The Redbook gives you instructions and the web that tells you how to submit, but this is different compared to other Offices and Centers because they regulate different things.

\_\_\_\_\_:

-Don't know that it can be resolved. Centers look at it from a regulatory standpoint. CDER has been more willing to accept current/state-of-the art methods, while CFSAN takes a more historical approach.

-They are not consistent because toxicology is used differently in the different Centers so they develop different methods for evaluation.

[REDACTED]:

Most of these are sensible reactions to different safety standards for different products mandated by the Act.

[REDACTED]:

Some offices may be territorial--protective of their area of expertise.

-This is part of the culture; however, one office may always be in disagreement.

-Even though we are all working for the same goal, it doesn't always seem that way.

-Need to be more open-minded: look out into the real world.

[REDACTED]:

-There are no templates. Are there consistent requirements for submission of raw data? If not, there is no rationale in today's world for inconsistencies in data format and submissions. Any data we receive from anyone should come in a standardize format so we can use it with applications and use meta-analysis and do more powerful assessments across studies that are being submitted. Would like to see somehow that this is linked into in some way so that even food labeling electronically. That requires a lot more authority than we have currently. Data standards are hugely important for us to conserve resources, for industry ultimately to conserve resources, to be intelligent and informed in our actions. It allows automation. We can decrease the number of people that are needed to massage data.

[REDACTED]:

Adamantly believes we must see submission of raw data and data tables. Because regulatory, we are already taking industry at its word on the veracity and validity of the data and we need to see that information. The absence of data doesn't allow data interpretation or new ways to do it: especially non-traditional applications, where you have a unique compound or concern for the compound. Looking at the data does not mean we won't come out with an interpretation that is of benefit to industry. If there are differences, they can have a discussion/dialogue about the results

- Understand the need for differences in the risk assessments, but for differences in whether or not we are asking for data, no.

[REDACTED]:

-Depends a lot on the nature of the data and information that are being submitted. There is a real difference between submitting raw toxicological data versus looking at the newer technologies where the methodologies have not been standardized. What is really important is consistent recordkeeping. Once you are consistent about record keeping you can always go back into the data and find what you need.

-We are now in an era where we need to stop looking at the OF versus Office of Drugs. They are the same toxicological questions. People are trying to knock down the silos between CFSAN and CVM, but where they really need to be knocked down is between the Foods Groups and the Drugs Groups. CVM is really a drug group not a foods group because the statutory authority under which we operate deals with drugs and there is a food safety component.

[REDACTED] [REDACTED]:

-We could do a lot better job coordinating. No one has created the avenues for that coordination.

## 5a. Is chemical safety research at CFSAN and CVM adequate in scope and scale and well aligned with the Centers' regulatory mission and priorities?

[REDACTED]:

- Not in terms of toxicology.
- In analytical chemistry, we have good researchers who are state of the art, and publish their research (methods for melamine).
- There is good collaboration with the lab.
- Yes. We focus on intake level and exposure, all from the intake of food. We are looking in the right direction for providing safety based on food intake.
- The lab people often attend at least one meeting of the chemists per month, where they ask if there are projects for them. Also, there is a contact with Moffit Center in Chicago (joint venture). They are currently working on a project involving migration data for them. They have many different outlets for help on actual data and utilize them as much as possible.
- FA has had more interaction with lab people: analyses and help with contracts; particularly on post-market issues; their contribution is critical to exposure assessment.
- Good working relationship chemist to chemist with our Office and the chemists in Wiley Building. Have a good idea on what they are working on. Cannot speak to the toxicology side of things. There are projects the toxicologists have interest in, but not clear how they pursue these interests. Chemistry is well aligned between the research group and the review side
- The chemists ask a lot of questions of each other, collaborating on projects, and have good discussions between the labs and the review team.

[REDACTED]:

- Works well when priorities are aligned.
- In general, yes. But there is not good alignment with the public health mission. A longer timeline is required for public health issues: chronic issues require a 10-year timeline; acute issues get attention, but this really isn't public health.
- For premarket approval, can require additional data. Can send a petition back for more data. We don't need to ask our in-house researchers for much data/information
- No. But it is difficult to carve out one area of research to explore over a longer period of time. The problem is vacillation in objective of the research. Research has tended to be affected by overall science process (tried to follow the mission, develop testing methods that are very useful). Need more time and more substantial monetary support.
- Yes, what's going on in CFSAN research and what's going on with CFSAN regulatory is not well communicated.
- They do research work for us but do not know how they prioritize the work. Personally never heard information exchange between research part and regulatory part.
- At CFSAN that particular aspect has improved dramatically. Previously the two groups that we rely on for our research, NCTR and [REDACTED], would follow whatever research they felt was important. Now there is increased focus on supporting the regulatory science. Especially within [REDACTED], and within the Center overall and NCTR, we are getting better.
- Don't think so. This is because the scientific base is weak. Need to change this first. There may be many ways to achieve this, but it is difficult to do this under the current organizational structure/hierarchy. Now, everything goes through a command chain, making everything management's decision.

[REDACTED] ( [REDACTED] ):

Don't know. There is no communication between centers.

[REDACTED]:

- The issue goes to scale, there are not enough people to handle all the projects and needs. Limited numbers of people and time constraints limit the ability to address new challenges appropriately. This additional level of focus and time dedication can be difficult to manage with regular day to day workload and requirements already requiring most of employees' work schedules.

[REDACTED]:

- In the sense we deal with detection and measurement [of chemicals], it is aligned with our regulatory mission. In the sense that we look at whether a chemical is safe and how you would go about determining if a chemical is safe,

then no.

At CFSAN, our toxicology chemical safety program was beaten up. [With the move of ] the toxicology group to this(b) (5) lab in Laurel, MD, there were no personal interaction between the regulatory people and the laboratory people. As consequence, with very few exceptions the staff in the lab was never made aware of the concerns of the regulatory people and vice versa. Very little chemical safety research has been done in CFSAN – most of it has avoided subjects of major significance and fails to address current regulatory data gaps.

:

Getting there with the Strategic Plan and Food Safety Programs. Before it was difficult to line up research with offices. There is consensus between research and upper management so that the needs of the center are outlined and the research is being adapted to these.

-No.

Getting better in in scope. Research at ORS and [ ] ties back in with program office needs, leading to better communication, which forces alignment, and setting priorities. Scale is tied to resources (personnel & funding).

-Within CFSAN, over the many years it has been inconsistent. We are the only Office within CFSAN that is not tied to a product or program. We are dependent on the program offices for feedback as to what the key safety issues are. Unfortunately many times this is not straight forward to get.

-No for CFSAN. The toxicology program was not well-supported for many years; that's a program they are trying to build it up again.

:

Yes. Difficult questions come in, and we have a process in place to handle them.

:

-Chemical safety research is trying to align with the Center's regulatory mission.

:

There is a conflict. People that are planning research like to plan for years ahead, but if you are a regulatory reviewer you might have a question that you need answered quickly that doesn't fit into their long term research project.

-With our Office of [ ], we do a method transfer trial. They show that a method that monitors for residues can be used in a government lab. We do about 3 of these a year. We have a good interaction with our Office of [ ] for those kinds of things. The other thing they have been good about is making themselves available and making their resources available. If we run into questions that it is unlikely we could get the drug sponsor to answer the question. They have done a lot of work with fish. In the last 10 years, incredibly responsive to our regulatory needs now. But historically (10-15 years ago) they were under the delusion or specifically promised that part of their time was for their own research interest. It's probably top to bottom that has changed in the past 10 years.

-Yes. We do not have a lot of money to dedicate to do research. Whatever money we have we try to focus on mission and answer certain regulatory scientific questions that are quite important for that particular time.

:

-The extent to which we choose to do additional laboratory-based research should be a function of satisfying uncertainties that may persist as the result of the assessment of a particular substance or class of substances. There could be greater work to align with NCTR and other testing organizations. We should not be spending the meager resources that we have and developing large research programs but instead focusing then on questions that are specific to regulatory questions.

[ ] :

-Yes, think it is. More could be done in terms to putting together an overall system, a systematic approach, to how things are done. There has to be more coordination and less stovepipes.

## 5b. If not, what are some examples?

[REDACTED]:  
Don't have enough resources to do all the research we'd like to do. Chemists are responsible for developing methods as well as doing regulatory analyses and regulatory research. Have needed to work with other groups to get things done (e.g., Moffett Center in Chicago; and National Center for Food Safety and Technology (NCFST) now Institute for Food Safety and Health). Would like to have more work done here. The laboratory group which formerly supported only chemistry now does work for everyone.

[REDACTED]:  
Particularly at CFSAN, there are consumer products that do not have premarket approval requirements. Some of these include cosmetic ingredients, dietary supplements and botanical substances, GRAS additives and ingredients. In addition, approved additives have no requirement to reassess safety in light of new data, even though many of these additives were approved long ago (BPA comes to mind).

-Within CFSAN research is spread through different offices and they don't communicate well. Might not know of differences.

-NCTR for many years had essentially followed their own interests in terms of research. That has started to diminish, but the culture does need to be addressed. The [REDACTED] of [REDACTED] is making every effort to eliminate that single way of thinking. [REDACTED] has come a long way. They brought on a new [REDACTED] that really made an effort to reach out to the rest of the Center.

-The special projects that come up: cumulative exposure calculations. Sometimes a compound we see is in not only food but within pharmaceuticals, the air (environmental), or cosmetics. So the question is what is our cumulative exposure? To draw that across different Centers or Agencies is very tough.

[REDACTED] (b) (5):

-Regulatory decisions mainly depend on animal studies. Need to do more clinical studies to make these decisions.

[REDACTED]:

-It's not entirely clear whether the Agency considers research on the safety of chemicals to be within its scope. The Agency seems to feel that it is up to others to do the safety research for things which are additives and GRAS substances where we have pre-market review of. When it comes to other types of contaminants not so sure it does or not.

[REDACTED]:

-Bisphenol A (BPA): People in devices were very interested in BPA toxicology for many years. But within CFSAN, they decided the chemists knew best and should not be questioned. They told the toxicologists that BPA was too controversial and the toxicologists were told they were not to work on it. If they were caught working on it on their own time they were strongly discouraged. (b) (5)

(b) (5)

[REDACTED]:

-There is a lot of research that would fall under the definition of public health that is not being done; you can't always see the contribution for a project at the outset.

-In the past, research projects have been found to be outside the scope of the current mission and were stopped. - Getting better at tying research back to regulatory needs. Help from upper management, not a priority and so shouldn't spend time on it.

-The [REDACTED] is under-staffed. They are missing out on having experience and expertise in multiple areas of toxicology. They are very strong in reproductive and developmental *in vivo* toxicology, and are developing strength in *in vitro*. But there are other areas, especially within *in vivo* animal research that needs to be beefed up. Another area we will be building in will be research to address issues associated with endocrine disruption.

[REDACTED]:

-It used to be that the labs and the food products lines were aligned. In some ways it is good to have the alignment of the group doing the analytical measures for the products you're working with to be in the same Office and communicating. It has continued because of historical relationships, but as people retire and new people come in I don't know if that is going to happen.

[REDACTED]:

-We have a subset of drug sponsors for minor use minor species that don't have any money at all. They are public sponsors. Rather than have them conduct the full fledged *in vitro* study which could take 3 months and cost the \$50K., we had our Office of Research get some samples from CDC and run a preliminary study. It wasn't

definitive, but it told us whether or not the level we thought would be in the tissues would have an effect on the bugs of concern. In the preliminary study we were able to conclude that we did not need the data and did not have to set a microbial ADI for this effect.

-One drug that was used to (b) (5) when moving from one place to another without causing injuries. This drug was used in human medicine for many years. We did not have the toxicology studies. So the rationale was that it had been used and is safe but we had some issues concerning metahemoglobin. The reviewer worked with NCTR to run a short group of studies to see if that was an issue and it turned out it was an issue. Because of that they have a dose response and were able to regulate and help wildlife. The aquatic species do not have a lot of money.

[REDACTED]:

-Antimicrobials. CVM has dealt with antimicrobials used in animals. The public health outcome is resistance to microorganisms. There is a loss of treatment when the infection occurs in humans because of the resistance to appropriate antimicrobial. CVM was getting some petitions for use of antimicrobials as part of ethanol production. CFSAN was also getting the same stuff and they were doing things totally separately from CVM. There was no coordination and there really should have been.

### 5c. What suggestions do you have for changing the scope, scale and alignment?

#### Inter-group comm.

\_\_\_\_\_:

-Chemistry talks well, but the respect of the toxicology side of things are working may be a place where we could look in to. Working better at aligning some of our interests in the regulatory side with respect to the labs. Not sure if the toxicologists or interviewee understands what kind of research they are doing up at \_\_\_\_\_ and other places.

#### Inter-office comm.

\_\_\_\_\_:

-Follow-through on both sides. Research can't shift with each issue.

-More feedback from upper management would be helpful is helpful; i.e., if a project is of lower priority, the lab should not be spending too much time on it.

-More personalities, than money. Ongoing issue now with dietary supplements, which we were primed and ready to start evaluating for toxicity. Getting minimal if any feedback from the program office that regulates the dietary supplements. We are operating in the dark. Have been here long enough to remember when the regulatory toxicology and research toxicology were in the same office. Didn't run into any communication problems.

-Reviewer's office should plan ahead of time of what their research needs are.

\_\_\_\_\_:

-Better coordination/communication between research and regulatory groups would be beneficial. Example: If there was a working group for everyone with an expertise in genetic toxicology comprised of both regulatory and research scientists. Working groups that overlapped in programmatic areas it would be a way for everyone to know what is going on.

-Need or improve communication between offices to determine what is needed. Need to know what they can do for us. Don't know capacity and capability.

-Main suggestion would be to ensure that the communications are solid. We need to communicate with the various research groups (\_\_\_\_\_ and \_\_\_\_\_. They need to ask us what we want. If we can't give them good solid answers then we have to work together. The communications have improved dramatically with both groups.

\_\_\_\_\_:

Need more collaboration: can become too compartmentalized. Can also cause a gap when they leave.

-Rotate people through different types of assessments or encourage more details so they get an idea of what or why they are doing things a certain way.

-For problems: if people aren't in your office, there is little recourse to challenge decisions. Especially chemical safety assessments should have input from different offices, some way of settling an issue (e.g., for one report generated by a single office, all comments from other offices and an external peer review were ignored).

\_\_\_\_\_:

-Have worked to be more transparent in showing what kind of research goes on at \_\_\_\_\_. The office can use Traciton to post articles, what you are working on. This has been helpful to show what is going on, determine whether it's relevant to mission, and may help to prioritize. A peer group evaluates research proposals to evaluate whether they are within the mission.

-Should always have the capacity to support to a certain small extent some immediate regulatory need while you are also developing these long term research plans. Make sure the researchers understand scope, scale, and alignment will be different for regulatory support research and their long-term planned research programs. It would be nice to see each other's perspective and get together to talk about it.

#### Center-wide comm.

\_\_\_\_\_:

Center-wide risk assessment effort accessible to all scientists when key evaluations are performed: something along the lines of "grand rounds" in hospitals.

\_\_\_\_\_ (\_\_\_\_\_):

-Conduct workshops to discuss issues.

\_\_\_\_\_:

Increase communication between research for CFSAN and CVM.

-The doors are open between [REDACTED] and [REDACTED].

-Starting discussion between [REDACTED] and [REDACTED] to discuss priorities: if grouped, they are more powerful, productive, higher quality of work will be produced; increase depth; share expertise.

-Decided based on first meeting - management for CVM and CFSAN researchers would meet monthly from now on.

[REDACTED] [REDACTED]:

-They have to set up the mechanisms to talk. There has to be a leadership exhibited by senior people to say “we have to do this.” This has to become a priority. We have to set up these mechanisms to coordinate when those chances come up. We have to break out of those stove pipes.

[REDACTED]:

You should gather experts in a room, the people that actually “do” the work, not the people who “think” they do the work or think they “know” about the work, and ask them. The mission should be clearly stated. Then you put your best people on solving the problems, instead of doing this top down.

## More details/training

[REDACTED]:

Every lab toxicologist at a master’s level or above should be assigned to do a 6 month training detail at some point (preferably soon after hiring for new ones) in a regulatory review branch. The lab folks need to know how the review folks function to understand how their research might fit into a regulatory review paradigm.

[REDACTED]:

We won’t be able to physically put the staff together, but when we hire new employees we want them to improve their technical knowledge and to better understand their role in the Agency. They need to do some rotations or details for a year or two after they come here so they get to see the way things are done in other Offices and Divisions and make some personal contacts. Regular interaction between the Toxicology laboratory staff and regulatory are necessary to breach this gap.

## In-house research

-It would be nice to have more in-house ability for post-market analysis; have had to contract out, but not always needed. Our labs have been helpful with set-up for contract work to see that we get what we need.

- There should be more emphasis on long-term impacts

[REDACTED]:

-If we could identify a data need and get some sort of turnaround time (within 6 months) without it having to be a major “top down” decision. It seems like if something is not “top down” it won’t get done. Don’t know how to convince someone my data gaps in a memo are worth the time and money.

[REDACTED]:

-FDA could be doing research on the safety of many of these substances (for which premarket approval requirements are limited or nonexistent) that would not be constrained by industry being responsible for the data. Could try to engage inter-agency and inter-government entities in this: NCTR doing more research on dietary supplements. Increasingly an inter-Agency effort with money supplied by NTP. Alt. methods from NIH.

-Sponsors are responsible for doing research. CFSAN only gets involved in assessment when it has been regulated (post-market). This needs to be done and in an organized fashion.

-CFSAN research should put more focus on evaluating and even validating some of the methods that are being discovered by external researchers: things that are being discussed at the [REDACTED] level and things that are coming out in primary literature.

-We could work a little bit more toward safety testing in children

[REDACTED] [REDACTED]:

-Most animal studies are inadequate: the studies do not reflect oral administration as food; therefore, we cannot get the answers we need. Establish a clinical research function within the Center. If current research is not meeting our goals, we need to move ahead. We need to do our own research to get the information we need.

[REDACTED]:

-There should be funding processes where people compete for funds based on the point of mission relevance. This is what NIH and academia do. If you do research you focus on where the money is and with that you get your priorities. There were mechanisms where they tried to streamline research which was the CART system. This is where every research project initiated in the Center is logged in and also a progress report of each project at various

levels. This has more to do with the hiring process. If you hire a researcher to this Center then it should be made clear that it is their job to do mission-related research and not their own little thing.

-The mission of the Agency, when it comes to research, changes faster than research can switch gears within the constraints of funding. Often there is a mismatch. Some of it is just a communication that the rules and regulations that pertain to the research may not trickle down as quickly as they should. The researchers are just not as flexible in terms of shifting from one thing to another when the mission's need changes. A lot is funding.

████████:

-This whole process of strategic planning and strategic goal setting isn't starting from the top in setting our strategic goals and having those move down to people and figure out how to meet them. Instead it is building from the bottom, what you think are some interesting things we could do in the lab and trying to turn them into goals for the Agency. Having a management more committed to elucidating the actual principles about what we need to do would help a lot.

████████:

-There needs to be a time division between follow-through on issues and exploratory research for novel ways of doing things, new methods etc. Even though not a basic research institution, there should be some time for exploratory research.

-Sometimes, due to the Food Safety Initiative, the lab misses opportunities to do research that they are capable of doing, but that is not strictly part of the mission (e.g., tobacco byproducts)

-Need to develop methods that can be used now; they are lacking validation of new assays.

-NTP, NTTR have Tox 21; we don't

████████:

-Relevance matters more than reliability. Researchers from an academic background think it is important to get the right answer about something regardless if it is relevant or not. A lot of times a rough answer to something we really want to know is better than being certain about something that is not that important.

████████:

-Each Office should have a research committee that works on a research plan for the next 2, 3, and 5 years. Scope is then clear and common and then can be aligned with Center priorities.

## Other

████████:

-For post-market issues, we need to defend our decision; get involved in the science portion. Lack of comment from FDA may encourage further research to challenge our position.

-Contract labs have worked, but need funding for this. Relying more on European data because they have more money for research and more people doing. For alignment, need more resources allotted to do chemical research here rather than at remote sites.

-Right now it's working; things are starting to fall into place now.

████████:

Chemists sometimes seem under pressure to (b) (5) ensure that FCNs get under some of the data requirement thresholds.

-They need someone in charge that is knowledgeable in public health and is out there and is reading and dealing with it. My suggestion is that there are outside reviewers of proposals (like there is for NIH) so make sure they are relevant: 1. What is the significance and 2. Have to display an in-depth literature review. Another way they have to be accountable is the people on top that are controlling all this need to start paying attention. Three scientists in our group that are being pushed toward *in vitro*, but the █████ does not accept *in vitro* data. I don't care if they say this is quick screening. That is of no value when you are reviewing a compound.

████████:

-Adjust the Science Policy Group within the Center to be more similar to EPA's Office of Regulatory Development (ORD) to handle special projects.

████████:

It may be more beneficial if we place money aside. Heard from outside that FDA never funds graduate students to work on projects, instead they just bring in ORISE fellows with the money and get the work done that way. USDA does a lot more funding of graduate school research.

████████:

-We need to build up █████ again which will require additional staffing and additional funds to bring in the needed

expertise.

████████: -Complaints from regulatory review supervisors need to be taken seriously. They will argue that the above suggestions will take their best people away from critical review tasks and thus make it difficult to meet review deadlines. Their point is valid and needs to be addressed.

████████: Need to evolve because we are seeing different ingredients. Different types of questions may need different types of data.

-Still rely on traditional data when we could be looking at different data

-When we approve an ingredient for one use, we may not look at potential uses; maybe we could factor these in based on projected uses.

████████: -We need to keep reminding people they are a regulatory agency, and they are here to do whatever their piece of the regulatory function is, and that's what they are being paid to do.

**6a. Are the program's risk assessment and safety evaluation methods (a) in keeping with the current and emerging state of the art and,**

[REDACTED]:

- For toxicology vs. Tox 21 need to figure out what we can use for our regulations, which are mostly cancer based.
- Yes
- Pretty much current. We use updated programs/consumption databases to keep up with changes. Maybe not state of the art . . .
- No. Felt the conclusions of the Pew Workshop were valid with respect to this issue.
- Yes (chemistry). Need to keep up with new methods. Don't always have state of the art info on what is coming out of academia. Follow what is new in Europe and the world and in industry. FDA drives methods for evaluating because they need to satisfy. Will look at methods from the outside as well. Try to choose the best. Trying to harmonize data requirements and testing methods between EU and the U.S. Have set up training courses (polymer chemistry), conducted an in-house analytical chemistry survey. Have up-to-date equipment; better than academia in some cases. They have embarked on a program in which they are revalidating their regulatory assumptions to make sure they are on track.
- Pretty much yes. We send recognized experts to JECFA and Codex. Our risk assessments are recognized. There are always new methods, but we try to stay current.
- Chemistry side is current with what they do with respect to calculating human intake values and human exposure to food additives. A number of the people in the office are world-wide experts estimating exposures. It's good but there is more to learn, new techniques coming out. We are aware of what these are and look at them best we can with the limited time frames and workloads we have.
- Yes, largely they are. We are not the most well-endowed in terms of equipment and resources versus other Agencies (e.g., NIH), but think the methods here are pretty good.

[REDACTED]:

- In keeping with current state of the art. For emerging, need more resources to stay abreast of changing science/methods.
- Our risk assessments and safety determinations are based on validated guidance and data requirements. To go beyond that in terms of emerging methodologies, we are aware and provide comments, but until they have been validated and can be meshed with the information that we ask for, they can't be used at this point. This is not where our mandate is at this point.
- Yes, to the extent that new/emerging methods have been accepted by the scientific community, beta-tested ad infinitum, and are part of the established safety paradigm.
- Yes. The core of the safety assessment is traditional toxicology studies (Red Book). Advances (QSAR, modelling) are useful to support/confirm/validate and/or screen substances.
- RA and Safety methods are in keeping with current & emerging state of the art, but not necessarily with emerging state of the science; they are limited by what you can practically do. Protocols and tests need to be validated to be adopted, but it takes more time to validate methods than to develop new methods, and the procedures are not great. E.g., common assays. We can't always use evolving science.
- Yes, pretty good at keeping an eye open for most updated technology, but must realize we are not doing cutting edge research. Can look at something others have done to see if we can use it or not. Not everything is useful
- No, but it's not entirely our fault. 1. We have a risk management group in place that is very adverse to change; and 2. We have a very laborious and time consuming approach to implementing new technology and new science into our safety assessment work.

[REDACTED]:

Not aware that they are. Risk assessment is based on exposure and toxicology data; he has no idea what they are doing.

Yes. In vitro methods to reduce use of animals. Examining what compounds can be grouped together based on toxicity (QSARS). Can apply available data to new chemicals, so do not need to request additional testing.

-Outdated. Certainly little internal guidance on endocrine disruptors. Need updated guidance on infant safety, especially for food packaging.

[REDACTED]:

There may be three areas where we are not aligned with emerging state of the art:

1. Risk assessment for carcinogenic impurities - we don't have a way to recognize the non-mutagenic carcinogens. For example at EPA, if they look at the mechanism of carcinogenic action and determine it is

not mutagenic, then they might be able to calculate an ADI. That would allow industry to have wider use. A carcinogenic risk assessment only allows very small amounts of use. So if an ADI were assessed then the industry might be able to expand their use. From industry's perspective that would be state of the art. But it may or may not benefit the consumer. From our perspective, we would prefer to do the carcinogenic risk assessment.

2. Low dose hypothesis - Agency is aware of it and may have published a paper on it, but currently we are not operating under this hypothesis.
3. Endocrine disruptors - currently our particular Division does not actively force the notifiers to screen for endocrine disruption. It's an emerging state of the art and sometimes the notifier will voluntarily screen chemicals for endocrine disruptors, but not always.

████████:

Not in keeping with the "state of the art" and in fact hardly consider it. Right now we just do the same things we have done for the past 30 years.

████████:

-We have the PhDs in science, but the other half, the math side is lacking.

████████:

-To be fair, while there is ferment and widespread feeling that the current state of the art is badly outdated and in need of reform, it would be hard to argue that there is as yet a new state of the art behind which CFSAN lags. There are many exciting proposals for new methodology and paradigms but as yet none have taken hold.

-When we need it and the data allow for it, we are moving in the right direction.

████████:

-Research is starting to be more state of the art: moving off from Redbook guideline studies to Tox21 approaches (biomarkers, reducing/replacing animal models). Some of the research is behind the times but proven; some of the new methods are more exploratory but lag in validation. This is just the "nature of the FDA"

-The program is trying to stay current. The lab has been well supported the last few years. Able to get equipment, etc.

-████████ is petition driven and so it is less state of the art than other offices. Microbial and pathogens risk assessments are more in line with state of the art techniques, and seem to undergo more significant external peer review. Not sure this happens with other offices.

-Yes, but we could improve. We recently acquired more sophisticated techniques and instruments. Yes, we are keeping up, but still the private sector will move faster.

████████:

-No safety evaluation methods are established because no premarket approval. No set established methods *per se*. Would be helpful to have more authority.

████████:

A regulatory agency can almost never be at the cutting edge of science because we are not at the cutting edge because you are not sure this is where you want to go. Must be a half step back.

-Can't require industry to take that risk.

-Need to know the cutting edge and when to pull it in. We try very much to be aware of what is out there via membership in societies and attendance at meetings; however, you can't put new science in place until you're sure it will work.

-We get a lot of complaints, because reviews of different assignments are different and because reviews are conducted according to the law, which hasn't caught up with scientific improvements. We try to maximize capabilities to catch up with science within the scope of the law

-Not necessarily. Need to take a more conservative approach to protect public health. Can only ask for certain data, and it is difficult to change the guidance.

-We'd better be using regulatory science that is well respected and agreed upon and well established. It's different than if you are doing research. We could do a better job of incorporating newly developing science into our arsenal of regulatory projects. Science for the 21<sup>st</sup> Century (Tox21) moving away from animal studies. For the last 20 years or so we have been working very hard on alternatives to classical studies but really haven't developed any suitable alternatives to the traditional carcinogenicity study, chronic tox study, the reproductive study, or the teratogenicity

study.

-We could do more modern things, but would take more time and money to validate the new thing. My impression is the cost to develop a new protocol to validate *in vitro* methods would exceed the cost of buying, treating, and killing 100 cows. Probably whether or not you are moving into new and novel technology pretty much depends on what part of the Agency you are in. As we move away in food animal pre-approval from a more traditional kind of drug to a more novel kind of drug we are trying to look at alternative approaches. For novel products (protein drugs and peptide drugs) we are trying to move away from a lot of our standard, “we’ve always asked for this, we’ve always asked for that”.

-Our work involves whatever the sponsors bring in. For the sake of their own company they are always keeping in step with the technology. So we have to keep in step with the sponsors.

[REDACTED]:

-Doing pretty good on this. There is an Interagency Risk Assessment Consortium (IRAC) that works very hard in involving everybody doing food safety risk assessment across [REDACTED], CFSAN, EPA, and USDA. CFSAN is a main driver in that.

[REDACTED]:

Ours are at the animal biotechnology group. Most countries copy us.

## 6b. (b) recognized as such by the external scientific and stakeholder communities?

Yes/no. Those who understand what we do think we do a good job with the resources that are available to us.

-Those who do not understand are more critical (e.g., Pugh and FDA vs. EPA exposure assessments).

[REDACTED]:

Yes. Most of the suggestions and criticisms are that we are too conservative (over-estimate exposure), but moving closer to reality.

-Yes for industry and scientific community. No for consumer groups and Pew

-Depends on the point of view of the group who is evaluating us. Even members of the Pew group, when spoken with individually or in small groups seemed to understand our point of view and how we do things.

-Yes, several people go out and work with international bodies; join expert committee on food additives, European Food Safety Authority (EFSA).

-The general public is another issue. They don't fully understand what FDA is doing and so there is an issue with transparency. Because of that the external scientific review community has more of the public funds so are more interested what the public has concerns with. Then they have the viewpoint that we don't necessarily know what we are doing and if we are doing it properly.

[REDACTED]:

-For this job, state of the art is not as important as whether it can be validated and accepted by the broad scientific community.

-They feel we're inadequately trained (re: new toxicology testing). They don't know why we haven't incorporated these methods into our testing procedures. We are trying to be more active [REDACTED]

[REDACTED] Feels this whole thing is based on a poor understanding of what we do and what the needs are for risk assessment testing.

-External groups don't always appreciate the value of the work that is done. They don't understand that cutting edge science won't work in a regulatory setting. Industry has better appreciation and understanding of what FDA does; consumers do not.

-No, there seems to be a misconception that FDA is not using the most current science. This comes from the fact that the new and emerging science has not been properly evaluated and validated. Often times it may be considered by the scientists but may not be the pivotal piece of information. Just because it's new doesn't mean that we automatically ought to be using it and adopting it. It takes time to make sure that these things are useful for the purpose.

-The risk assessment or safety evaluation process needs to be more transparent to the public to avoid misunderstanding and confusion. If they know what kind of measure and what the standard we used there would be much better understanding between the regulator and the research scientist. The academic scientist does not understand how we work; is not familiar with the regulations.

[REDACTED]:

-By law, when these companies submit data to us they are supposed to submit all of safety data they have. But what frequently happens is (b) (5) [REDACTED], they

don't give us that data. They recognize what we do (b) (5) [REDACTED] and take advantage of that situation.

[REDACTED]:

-They are more criticized than recognized because we have methods to evaluate risk but often these methods cannot even be applied successfully because of some legal restraints.

[REDACTED]:

Yes and no for both. For example, rapid detection methods for toxins/contaminants in food are recognized as important in Europe but are not addressed here.

-Individual researchers are recognized by the external scientific community (nationally and internationally) for their work in nutritional and food sciences

[REDACTED]:

Mixed. Academics: no. Industry: mixed, depending on advantage. They have a better idea of where we're at because they have more information.

-It would be interesting to have information on what we do not approve as easy to access as information on what we do approve. This could improve the quality of what we receive.

-They respect the scientists (education and background), know we're doing our best and trying to be innovative and will try to work with the Sponsor.

-Yes, have harmonizing groups like PICH that we are on and JECFA that feeds into Codex. We're working with other countries, groups, and industry.

-Both CFSAN and CVM are effectively harmonized internationally through JECFA. CVM has monthly meetings with EMA and the Canada regulatory agencies. We are involved with Codex and OECD. We keep tabs on what EPA is doing. We are not that dissimilar on how we scientifically look at these things in a regulatory setting.

-(1) The more novel the product the more likely you are to think we are stuck in the Dark Ages. The sponsor needs to catch us up. For novel product we don't look like we are up to speed. We are trying to be better, but we don't look like we are particularly innovative or flexible; (2) For more traditional products (especially in food animals) - sponsors are happy to do exactly what they have done in the past. We publish an FOI for every one of our approvals. Sponsors can see exactly what their competitor did when they got their product approved.

[REDACTED]:

-That's hard to do but a lot of the CFSAN people present at scientific meetings and that is where they engage stakeholders. There is an effort to try to do that. There are a lot of politics that interfere with engaging with the stakeholders.

## 6c. If not, what are the shortcomings?

### New methods

[REDACTED]:

Unwillingness of management to improve safety and risk assessment evaluation methods.

-Lack of knowledge of what's out there. Currently revalidating the assumptions we've made over the years (e.g., food processing conditions: have they changed? And how does this affect the food additives situation. High pressure sterilization). Feels they are chasing industry on changes like high pressure sterilization when industry doesn't think to bring them to the attention of FDA.

-Industry can go to certain law firms and get justification for not going to FDA; however, the issue of safety is arbitrated by FDA, not industry. This is making certain new food additives harder to track.

[REDACTED]:

-Although there may be many yardsticks for doing a certain assessment, alternatives are not considered. There is a lack of willingness to explore accepted alternatives that have not been done here before. No time allowed to convince managers, etc. of merit of alternatives.

-Toxicology and "Safety" evaluation have been undergoing a paradigm shift for over a decade (Tox21). Much of the world is engaged in the machinations of such a shift. But, CFSAN/CVM has not been part of this dialogue until recently, perhaps because the need to replace the "Safety Paradigm" has not garnered much enthusiasm in the seat of its creation.

-Many new programs are directed toward a specific tissue or time. This is OK if you've done the early general work to focus in on that tissue and need a more detailed assessment. A battery of in vitro tests will not give an adequate picture of what happens in the intact animal. If this happened, it would be by accident.

-Regulatory science demands that a toxicologist have that cohesive and interactive assessment of the toxicology in the animal mode (can be enhanced with clinical testing). We can't insist on clinical testing without specifically and substantially defined data gaps.

-The major shortcoming is that other Centers (CDER and Center for Devices) are more proactive in trying to get new science incorporated into the safety assessment paradigm, but our Center, for whatever reason, has not managed to accomplish that.

-Transitioning to new technologies always takes time because of validation and paper work and harmonization.

[REDACTED] (REDACTED):

Need to get people into the Agency to discuss new methodology, so that we can evaluate whether they will help us in our mission.

-We need to constantly be training our reviewers in these risk assessment practices and the current state of the art practices

[REDACTED]:

-In CFSAN, there are a lot of types of data, more mechanistic types of information, that have been standard laboratory protocols for 20-25 years that we have no guidance on and we never ask anyone to submit that type of information. It's basically biochemical information; we have tests now that we can look at that will tell us about an adverse effect that is beginning to happen and you wouldn't know it by looking at gross animal pathology.

[REDACTED]:

-The shortcomings of our evaluation methods are that often we are not even able to apply them, especially in the context of food because we still have the Delaney Clause.

[REDACTED]:

-The expertise to generate the data needed is not available within the division; need more help. Can do whole animal screening for safety assessment and looking at all functional organ activities. Need to have a genomics component to publish. At least need to be able to understand this type of data.

-It is a function of the organization: Can't forge ahead without background knowledge. FDA needs to take a conservative approach: e.g., (b) (5) better methods, find more.

[REDACTED]:

Have not progressed from 20-30 years ago. This is fine for many ingredients, and the existing safety assessment for allergens is adequate.

-We are doing a good job for some things, but we need to be forward-looking for others. For risk assessment of allergens already in the food supply, we need to do better.

[REDACTED]:

-If the government sector research can push how quickly this part is catching up, it will help align scientific

developments to the regulatory requirements. For risk assessment, CVM has risk assessment specialists who lead different projects. This has impacted on the improvement of reviews and the quality of our approach. This emphasis will play an important role in the future.

-New and emerging technologies: CVM cannot bypass the scientific community in dealing with these issues.  
-CVM has been good by allowing people to go to training and keeping up people's expertise. Professional training and conferences to keep us up to date. Get familiar with novel techniques and novel products. This may wax or wane because of adequate funding.

[REDACTED]:  
-There needs to be some serious consideration into things such as underlying assumptions of the mechanisms of toxicity: whether or not we need to be relying so heavily on linear low dose extrapolation if there is an assumption of genotoxicity. We need to look carefully into mechanisms so that we can determine whether or not there are thresholds. We need to publish more on general issues associated with the interpretation of toxicological data and alternatives to 20-year-old approaches. Also, we have to be careful about jumping on the new molecular studies, microarrays and things like that, because those still tend to be done in very few species, they are not very well validated, and we don't have a large end.

## Communication

-Inadequate info is relayed to the consumer. Need a good PR campaign.  
-Need better transparency: the Agency does not explain well what they do.  
-Communication problems with the public. The best spokesperson is not always put forward to speak for the Center.  
-It's a communication problem to the public and an education problem of scientist stakeholders. We do a great job of communicating our approach to stakeholders in industry because they understand what they need to do. Scientists from academia could benefit from more education in terms of what the process is so they can feel like they are not being marginalized.

[REDACTED]:  
-Shortcomings include a lack of understanding of the regulatory assessment process by the external scientific community. This could be due to lack of communication or engagement by CFSAN. There is also a lack of understanding on the purpose and timing of the validation process. Also, the lack of resources and time needed to keep up with these areas.

[REDACTED]:  
-We have our priorities right but communication needs to be improved. We will never completely satisfy the external scientific and stakeholder communities, but we could do better at communicating so at least we are a little bit closer.

[REDACTED]:  
Also, communicating with external audiences is important. The researchers do that by publishing manuscripts, going to meetings and presenting posters or presentations, or serving on panels. There is still a need for more communication to our external audiences.

[REDACTED]:  
-In general we probably need to interact more with stakeholder communities. When we are right we need to explain that we are right and when we're wrong we need to admit it. We need to provide an explanation.

[REDACTED]:  
The shortcoming of the whole system is you can get toxicologists to sit down and agree that EPA's decision is essentially the same as our decision and essentially we evaluated the same study. But sometimes the bottom line numbers are different and so public does not understand that. So we do not do a good job at risk communication. We don't do a good job telling the public where these numbers came from and what they mean.

## Int/ext peer rev.

[REDACTED]:  
The agency could do a better job of engaging with stakeholders.  
-Increased internal and external peer review would increase transparency and could improve methods.  
-From external sources could get data sources and identification of gaps and additional data to be included.  
-Research can fill specific data gaps, leading to fewer assumptions made in determinations. Need to improve link-back of assessments to the research component.

-They do not present at national meetings. The vast majority of abstracts that I've seen here for Tox are presented locally at our forum. So there is no scrutiny. You need to get negative feedback, you need to be questioned and criticized.

[REDACTED]:  
-Could have more outside experts involved. It should be easier here because the drugs are not as high profile, because they usually come here after they've been tried for humans.

### Funds/staff/time

[REDACTED]:  
-Allowing employees time to keep up with emerging state; now you can only work on current crisis.  
-Methods] Other than the computational toxicology group in [REDACTED] there is little attempt to keep up. The leadership position gained when Lehman and Fitzhugh from the Bureau of Foods invented regulatory toxicology in the 1950s has long ago been lost.

[REDACTED]:  
-Need funding to calculate exposures.  
-When you shift priorities, timeliness is an issue. The time to get data or a method out is not as quick as it could be. We do not have the redundancy built in that if someone is pull off a project someone else can carry it forward.

[REDACTED]:  
-We have difficulty to keep up with the state of the art because of the funding and the staffing. In today's budget conscious world it will take time and probably won't get up to the level that is really needed.

### Other

[REDACTED]:  
-New areas and databases should be explored (e.g., label and market survey data), especially in the post-market work.

-Those shortcomings would be parochialism.

[REDACTED]:  
-[Methods] Sometimes we would like to do a partnership for collaboration but there are limitations. Like how we deal with the private sector. You have to put the recommendation in place. That limits us because the private sector has the state of the art technology.

[REDACTED]:  
Depends on the project. Some get high visibility in a short period. Others take longer. Others backed by science credentials based on publications or recognition within professional societies.

-The Agency isn't putting in the kind of research effort that others (e.g., institutes devoted to this) are for major chemical assessments.

-Research should be done as one group; a centralized research activity. Could FDA do this under one umbrella, work under one Director. Separate from review office.

[REDACTED]:  
-It varies, from both how state of the art it is and how recognized it is. For a lot of the things we do, the scientific community consists of other regulators like us. So in a sense there is not a huge external group of people who evaluate these things independently of a regulatory nature from agencies all over the world would do. It's an inbred field.

[REDACTED]:  
-Too much input from legal/policy. Science may take a back seat to policy.

-Need more risk managers in some areas who can resolve issues, especially discrepancies between groups.

[REDACTED]:  
-It's problematic because in cosmetics we have to prove the problem because we can't require industry from a compliance standpoint to submit data. We have to show or demonstrate all the health hazards and all of the effects based on the amount of authority we have over our industry. The "burden of proof" is on FDA in a program with limited resources.

[REDACTED]:  
-[Methods] More can be done, but as an Agency, we don't necessarily need to keep up. Industry can push the bounds. We are result-oriented because we need to establish safety. Cannot embrace every new technology.

## 7a. What do you see as some of the emerging issues and questions in chemical safety review?

### Nanotech

- █: have put out some guidance, especially for FAs
- They have done more work at CDER, but the advance is more cautious on the food side because need to establish that it will do no harm.
- The public has a negative perception about nanotechnology
- How to view and define these cptds.
- █:  
But cosmetics have changed drastically. New claims. With nanotechnology and nanoparticles it's a different world now.

### Allergen thresholds

- Need to do a better job of understanding threshold response vs. safe responses; these are not necessarily linked.
- Another is allergen thresholds - methods are behind.

### Endocrine disruptors

- Do we need to re-evaluate the review process for specific types of chemicals that have raised issues (endocrine disruptors)?
- How to screen for endocrine disruptors? How to recognize endocrine disruptors? How to prevent them from entering the food supply?
- New issues have come up (e.g., endocrine disruptors) that are not just environmental issues any more. The toxicology, microbiology, physiology, and pharmacology fields are getting involved; these issues are merging together.

### Methods/technology

█:  
Current animal-based testing is insufficient. It is the Gold Standard vs. other in vitro tests; however, there is a gap in the area of human effects (e.g., Alzheimers, diabetes, etc.).

- QSAR for predicting risk
- How do we handle and use the new data. EPA has the new Tox 21 Project: will be testing some 8,000 chemicals across several new quick screening assays. What do these new tests mean? How will this be integrated into a safety review? Can this be integrated into a safety review? What will we do with the results of these new tests?

█:  
The standard toxicology paradigms are undergoing major changes due to advances in human genomics.  
-FDA is keeping Tox 21 in mind and is working towards that goal.  
-But cannot throw away the time-tested processes because we need to be more conservative.  
-Tox21: in vitro vs. in vivo models. Allergenicity. Epigenetics (based on in vitro methods). Need to see where these fit in our guidance before investing our time.

-Animal Alternatives can be considered in our existing regulatory context as part of the case-by-case, weight of evidence approach always harkened to but not discussed much in how to do solidly with transparency and peer-review.

- Whole paradigms are being scrutinized. Was recently addressed in the Strategic Plan.
- In vitro methods (appropriate use)
- The major emerging issue is the move away from animal use to *in vitro* studies for safety assessment and high-throughput screening methods and in silico methods, the TOX 21vision
- Side-by-side comparison *in vitro* assays with whole animal.
- How to: evaluate safety data, evaluate the safety of our proposed additives with less data, evaluate it not using animal testing, incorporate risk assessment procedures in our safety review, conduct safety reviews more efficiently? With limited toxicology resources, how to conduct pre-market reviews and post-market reviews in a timely fashion?

█:  
-TOX 21 issue with EPA; they are doing their TOX 21 testing. That stirs up a notion everywhere and in every

scientific community of what does animal testing and *in vitro* testing really mean in terms of human health? There is a lot of disbelief today that the Agency uses animal testing correctly in order to predict human outcomes.

████████: -Tox 21 (move to *in vitro* testing to reduce animal usage). Tox 21 is an area that is emerging and very important for us to get involved.

████████: -Methodology used for dietary exposure.

-The old “safety factor” paradigm is sure to be replaced with better ways to estimate uncertainty and extrapolate from animal and *in vitro* data. While toxicogenomics and computational toxicology shows promise, they will not be the entire solution.

████████: -Keeping people up to date, making sure people are familiar with the technologies.

-Validating analytical methods across agencies and other countries.

What about the -omics?

████████: -Whether or not: batteries of molecular tests are indeed adequate without some intervening physiological assessment; rodent models can adequately address some of the complex physiological questions we are looking at; there are other large animal models that could be used sparingly; use of animal clones where you get rid of inter-individual variability and outbred populations can provide you with more information on variability and uncertainty.

## Mixtures/groups

LMWOs (low molecular weight oligomers): e.g., there is a polymer ingredient that goes back so far that no one knows exactly how much the public is now exposed to and a closely-related ingredient that has been broken out separately to keep the toxicity limited to one and not both, when both might reasonably be considered together. A market-basket survey is being done on the one and not the other which seems to restrict the views one will gain from the survey.

-Evaluate group with same MOA vs. product by product. Instead of looking at just one food additive, look across the board at all current uses. Aggregate vs. cumulative risk assessments.

-Mixture toxicology (also of concern per NIEHS, NAS). Because NIEHS included mixture toxicology in its Strategic Plan, it will certainly be a big issue in the years to come. We need to be part of this. In a mixture, the effect may be additive at least or possibly synergistic. If we know something about the biological effects, not just toxicological effects, we can better evaluate the safe level for this compound.

-A risk assessment is made for a particular individual chemical, but in real life we are exposed to multiple components and microbes (chemicals, nanoparticles, bacteria, drugs) at the same time. Should look at the effect of the mixture of multiple components and how that effects the final risk assessment.

An emerging concern is low molecular weight oligomers. [When you make a polymer, which is a repeat chain of oligomers, they tend to be very long. But when they cycle back and polymerize on themselves then you might end up with a dimer, trimer, or tetramer. So that is what a low molecular weight oligomer would be. The long chain wouldn't be absorbed or migrate into your food]

## Botanicals/Supplements/Non-traditional Entities

There is a growing use for botanical/natural substances: although it is automatically implied that these are safe, not enough safety studies have been done.

-Functional-type food ingredients (mostly botanicals/naturals); much more complex and variable substances.

-There is a misconception that FDA looks at the benefits, in terms of biotech and GRAS. We are only looking to see if something that is added to food is it safe to food. We are not looking to see if it's going to cure cancer. That is not part of our mission. This story needs to be told more. (b) (5)

-Excessive nutrient access (Na, phosphates). They are talking food, not dietary supplements. They are saying get your nutrients from food, don't rely on dietary supplements.

-Foods with health claims; contaminating toxins contributing to disease (obesity, cardiac disease, diabetes, Alzheimer's).

-Safety of dietary supplements. By the regulatory nature there is no pre-market safety testing that is required, so the statutory burden is on FDA to show the lack of safety.

-The use of dietary supplements. Their use is widespread in public and they are not regulated.

- Biologically based drugs (proteins; large molecules/organisms)
- Non-traditional entities as opposed to traditional drugs: biologics, anti-virals don't fit the typical flow chart.

## Sensitive/susceptible pops

- [REDACTED]:
  - Seems there is a balance between the two topics of how to get a good image of usual intakes over a life time versus how to account of the people that are highly motivated to consume specific products at various stages of their lifetime
- [REDACTED]:
  - Elderly and infant toxicology. For elderly, specific to chemical safety as opposed to nutrition, where more work is being done.
- Sensitive populations: does current safety assessment capture the risk to these groups?
- [REDACTED]:
  - We don't look at sensitive populations (especially for adults undergoing chemotherapy, with special diets (gluten-free diet), and the elderly)

## GE Orgs

- Stem cells, genetically engineered animals,
- GMO (genetically modified) species: are they the same? Will they react the same to drugs? We need to get more involved with this.

## Post-Market

- [REDACTED]:
  - Post-market area. Post-market exposure assessments can take a long time because industry is reluctant to provide information concerning uses/how much use
  - Also, old materials that were replaced by something like BPA, but are now being put back into use.
  - Post-market surveys for additives (as identified or cyclic review)
- [REDACTED]:
  - Post-market: still trying to deal with post-market issues in the old way: chemists do exposure assessments, toxicologists do safety assessments. There is no chance to comment on each other's reviews or ask questions, and they are discouraged from doing so.
  - With problems like BPA and thiates/phthalates, we need to find alternatives to replace them if they can't be used. Need to find right alternatives-- some do not have enough data to prove they are safe. If we approve, will have the same problem all over again.
  - Post-market. We approved the chemicals then to outside found some above the safety limits. We don't have enough funds to analyze food samples; therefore, we cannot verify their results.

## Low-Dose

- [REDACTED]:
  - Too many chemicals have been approved for use without characterization of their ability to interact with biological systems. We have only focused on toxic effect at high doses, which are not usually encountered. A compound with toxic effects may go through because it is not expected to be used a lot so will not reach these areas.
- [REDACTED]:
  - We have good understanding of short-term benefits but not of long-term effects.
  - Long-term vs. short-term exposure.
- [REDACTED]:
  - Low dose hypothesis
- [REDACTED]:
  - Complex mechanisms of toxic effect: We now know there are biochemical mechanisms through which these effects occur such as induction of enzymes producing increased metabolism and alteration of metabolic paths for hormones

and drugs. This is well understood in the scientific community. Certainly CDER understands this very well, but we do not take advantage of this at CFSAN. We have no guidance on it. No one at the management level has encouraged anyone to go back and learn about this.

■: -The carcinogenic effect of additives. We have a decent understanding of the acute effects, but it is hard for us to see the long-term effects.

■: -Long-term, low-dose exposure. It is difficult to evaluate these data from new technology (genomics) and bring them into the risk assessment and regulatory process. Don't know yet how they will be applied or how applicable/beneficial they will be.

■: -How do you handle long term chronic exposures versus short term acute exposures?

■: -For chemical, do high exposures actually predict for low exposures?

## Other - Risk Assessment

■: -Risk assessment: Referred to NAS study: Risk Assessment in the Federal Government, Managing the Process/Progress. Academia identifies risk, sometimes does dose response but in an isolated system. It is incomplete and inadequate, don't determine exposure and can't evaluate risk.

■: -Need to incorporate more ideas from risk assessments: exposure considerations; try to predict better (we stick to 95% of populations, but there are different hazards associated with acute vs. chronic exposure)  
For analytical methods, with more and more data coming out, can start to do more risk assessment-type evaluations of chemicals.

■: -The lack of money of sponsors to invest in lots of animal studies; the desire to use a risk-based weight of the evidence approach for agencies and questions that haven't traditionally used that; and for a way to develop that is consistent with our safety standard to set an ADI (acceptable daily intake). Learning to talk risk-based instead of safety-based when we talk about human food safety. We have done safety assessments instead of risk assessment. We need to integrate the two and move toward risk assessment when we can.

## Other

■: -Active food packaging. New food preparation and processing techniques (new techniques for fresher/more natural food). All need to be checked.

■: -FDA does not have a great understanding of immunology. Example: Ingredients to bolster the immune system.  
- The amount of ingredients that is in a product: this is not tested from the shelf.

■: -Don't have mechanisms to routinely go back and re-evaluate our previous analyses, and look if new data will change them. Many of our previous analyses are based on consumption and usage estimates that were put in place when we did the initial review.

■: Identifying what you want to look at: chemicals are more difficult than bacteria.

■: -Developmental neurotoxicity adverse effects; neurobehavioral effects; epigenetic issues.

■: - Precautionary principle vs. dose response: just because you can detect it, doesn't mean it's bad. With modern analytical chemistry techniques can detect carcinogens (that we may have been exposed to for centuries) at much lower levels; these probably can't be eliminated. This becomes a problem with the Delaney Clause.  
-Consumer awareness as to what their purchasing/what goes into their food products and the origins and sources.  
-transmissible spongiform encephalopathies. Some emerging issues would be some manufacturing process that can be used to break up the prions so that the meat and bone meal would be safe.

-Consistency across agencies and countries in terms of safety; safety importing food from other countries (leaning more and more toward harmonization); organization of databases - integrated systems within FDA

[REDACTED]:

How do you do dose response curves for pathogens? It's hard to do a classic chemical safety review on a pathogen because you don't have the dose response data; pathogens are different from chemicals on how you review them.

How do we tackle genomics?

-What are we going to do with these byproducts from agriculture that are going to be fed to animals after the primary use has been made and you are left with this plant residue (e.g., algae for biofuels).

## 7b. How well do we facilitate the needed developments in the science to address and answer these issues and questions?

■: We do our best: reach out to industry, but then we have to wait for data (1-1.5 years).  
-Stuck in the middle between industry and consumer groups.  
-Industry needs to be more forthcoming.  
-Pretty well. At the senior level, when they talk to industry and trade organizations, may note a certain issue with some level of concern, can lead to a meeting for someone to come in and discuss that issue. Keep up with industry so we can ask intelligent questions. The lab does the same thing on their end: share info between labs and reviewers.  
-Case-by-case: QSAR was facilitated and supported within the group; however, we may not always be looking for other emerging technologies. May occur at higher level.  
-If they are asking how well does management facilitate us working with or collaborating with EPA or looking how we can use these new tests or how we handle these mixtures, we could do better job at that. We do have some collaborations with Tox 21 as well as other groups or individuals working on these issues. It comes down to being able to identify point people. Can we identify someone else from the other research departments within CFSAN or within FDA to help us address this?  
-As a scientist we publish and attend meetings but we have our constraints. Sometimes it is lost in translation because we are concerned about the legal aspect. We do facilitate it but there needs to be more.

■: -Group is progressing in the right direction, but need more resources.  
-There should be interdisciplinary assessment of all accessible useful information from all sources and disciplines, not just from high tech-based data.  
-The regulatory barrier between chemists and toxicologists should be minimized to embrace emerging issues and look at them on a practical level: e.g., to look at impact on different populations.  
-This is not our job on a day-to-day basis, it's an academic, scientific field, big picture question. We must abide by the guidance put in place by our management.  
-The time clock is a problem for special topics. Trying to work on some of them. Maybe a separate half of the group to work on special topics/side projects.  
-Not well. There are a host of scientific and policy issues that have not been addressed at CFSAN, and presumably at CVM, because of the reliance in the old paradigm. We have not been engaged in the dialogue.  
- We do adequately do very well. We have been conservative and quick, spend time, hire staff where needed to address issues, train as necessary.  
- Access databases to get the information we need. Go to workshops to familiarize ourselves with the major issues. Work with industry to find out new methods they have to solve our problems.  
- Not doing as good a job at facilitating the science. There is an outreach issue with industry, trade associations, and the scientific community to get expertise. The problems are from the administrative standpoint: trying to get the data or appropriate personnel on board. May not be accomplished in time. The process needs to be streamlined.  
-Until we have a more liberal approach to using current technology and science, we are not going to be able to address some of these issues. We need to be more proactive rather than reactive. We have a culture in place and often our risk managers are not the people that understand the safety issues. Also: We pay lip service. We get involved with groups like the International Life Sciences Group. We sit on their committees and get involved in some of their workgroups. We put on a good show but it's often not particularly effective. The Groups from the other Centers seem to be much more active and more willing to take a chance on new technologies than we are [based on need to have "presumed" safety for food].

■:  
-For BPA yes: worked with ■ and ■ and 10-12 grantees in academia for novel studies on low dose effects.  
-We don't do this well. Some contribution and some participation in TOX 21. It would be better if the entire Center would be much more aware of it and more a part of it. This is the problem with each and every issue in the Center. There are just a few people who deal with a few things; do a little here and there. The majority of the people don't know. There should be people as liaisons on these committees that are Agency representatives on all the workshops that are going on about that topic. It should not be just one person who then fails to communicate with the rest of the Center. It should be a broad representation.

■■■■■:  
-We can't just completely halt approving something that is coming in while we figure out carcinogens. There needs to be some healthy balance. We can improve our communications when we are taking this all into consideration, while we try to get further data on long-term effects.

■■■■■:  
-Usually address on a case-by-case basis. E.g., arsenic in apple juice. It has been present there for a long time, but now we are investigating the long-term exposure. Do a pretty good job of this (meeting as the needs arise), but it is difficult to anticipate and don't have money/manpower.

-Participating in addressing issues, yes. But there is a dichotomy between what upper management says and what is being investigated at the bench-top. Scientists go to meetings, read journals, clinical research forums to come up with research ideas. Not always true at the top. There is a big dichotomy between what is perceived as public health by the public and what is happening at the bench. The people at the bench would like to jump into these issues.

FDA does not facilitate development in the sciences at all. Need to have scientists engaged in external activities (e.g., training, attending meetings, learning state of the art techniques and technologies). Other agencies appear to be more in touch with emerging issues (i.e., EPA). Looks at how EPA does risk assessments.

-Through collaborations with outside scientists, seminars, workshops, symposiums, but again it is tied to budget.

-Mixed bag: As we recognize these topics then we start putting together groups responding to them. So we have nanotoxicology super group. We are trying to form a toxicology super group. These super groups meet at different Centers and get together to talk about the issues and keep each other informed. The other issue, Tox 21, is something we are not addressing well right now but we need to move toward.

■■■■■:  
-We need to develop a deeper toolbox for toxicology testing paradigms that are more targeted, pay closer attention to dose response in the relevant areas of the dose curve, and provide better extrapolations from in vitro to in vivo and from animal to human.

-One big problem is that there are so many layers of review, it ends up being censorship, by trying to please everyone you end up saying nothing.

-We don't facilitate the development in the whole area of toxicology. May be some work at NCTR does. In the Center, we address the issues as they come up and don't contribute to the development of it.

■■■■■:  
-Much of this is research: need more communication with ■■■■■. Have them do more policy-focused research. May need more outreach both ways.

■■■■■ is not a research-driven office: it can be done, but it is difficult.

-Strategic Plan has been helpful, especially for allergens: more focused research with a public health goal.

■■■■■:  
Collaborate with industry on CIRs (Cosmetic Ingredient Reviews)

■■■■■:  
-Make an effort at CVM to work on facilitating. Do a reasonably good job as an organization. There is support to look outside the box, but difficult to do if you're working under a deadline. The will and the tools are there, but the opportunity to access and use them is not. Need staff and time greater than the workload to have time to think. Have done a good job of recognizing nanotechnology and working across the Centers.

-Sometimes very well: on the issue of melamine, CVM was recognized as having reacted with lightning speed and transparency within 2-3 weeks.

-CFSAN has a risk-based assessment program that targets investigative field to assess/evaluate upcoming problems to assess how much they will impact (b) (5) ■■■■■. Using the risk assessment approach, we can identify toxicology issues and address them from a regulatory standpoint, rather than from a biological standpoint as we do now.

-There is a difficult balance with ongoing work. It is limited by resources. Now prioritizing "mission critical" projects, so emerging issues get moved down the ladder. This is all right for now, but could become a problem in the future.

There is a great push to begin to address these issues. Technology teams/different working groups.

-The process is starting; there is a willingness to tackle just about any new issues.

-There are various initiatives underway: one for innovation: new working groups of experts from across offices/divisions to consult on novel products. We are trying as best we can.

-It is not FDA's role to advance the frontier of science: this is for the research community; we adapt.

-We really can't facilitate needed developments in the science. The most we can do as regulatory scientists is participate in review of the newly developing science and figuring how to incorporate it.

-In recent years CVM does a good job. We may not have the funding to keep people as current as we would like.  
[REDACTED]:

-This is strictly limited by resources. We have Office of [REDACTED] ([REDACTED] is CFSAN and [REDACTED] is CVM) that do a pretty good job. When you have limited resources a lot of what they are doing has to be linked to the rest of the organization. The [REDACTED] of the Office of [REDACTED] ([REDACTED]) has done a good job to reach out for help in identifying what are the things we need to know about, what new methods we need to develop, and where the new technologies fit in.

[REDACTED]:

-We don't facilitate them particularly well at all. In large part that is because you have to make it an Agency imperative to do so. This is a long term project. You need to assign adequate resources (both in time and treasure).

## 8a. How can we keep the Redbook and other guidance up to date with the pace of new science?

### Comments

[REDACTED]:  
The group updates their guidance documents; however, it may take months to make a small change (Level 2). For Level I, it's tougher. Hard to get things cleared (b) (5) [REDACTED]. By the time it is out, it is no longer relevant.

[REDACTED]:  
FDA trails behind because of the need to be conservative to protect safety.  
-Scientists need to keep up-to-date with methods, then have an internal discussion on what can be integrated and what can't.

-For dietary exposure, we do a good job of updating the guidance (e.g., for calculating exposure). Improving the language for describing procedures. Believes this is done in a timely fashion.  
I-t needs to be updated, but there can be a problem with updating. Attempts to simplify or eliminate the requirement for animal testing may result in allowing less toxicology data to be submitted in support of a new compound.  
-Chemistry has its own guidance documents. Did a major over-haul to update on a 10-year cycle. Trying now to review every 5 years and implement changes as needed. Needs to reflect new analytical methods and databases.  
-In terms of the Redbook, do not know. In terms of guidance in our Office, we tend to have an open-minded approach to the various approaches that companies come about for making their analyses of various impurities or substances of interest to be used as food. We don't have a standard, i.e., this method has to be used to analyze this type of compound. We are more open-minded about what type of analyses to use. They do need to verify the analyses and have it properly validated. Because we have a loose guidance, new methods are being submitted; therefore our guidance does not necessarily need to be tweaked.

[REDACTED]:  
-Immunotoxicology is nearly absent  
-It does need to be updated, but requires continuing effort: it can't just be revised and done.  
- Until new science has been validated and accepted and we're sure the methodology can be utilized correctly within a day-to-day science review for risk assessment, there's no point in trying to force it into Redbook. Pace of science may move quickly, but that doesn't determine how that relates to everyday food safety issues. Somebody needs to make a case for the new information being equivalent to or better than what we have been using/receiving in terms of risk assessment.  
- Can keep it up to date when new technologies/safety research has been accepted by the scientific community at large, thoroughly tested, and established that it reflects the correct endpoints. Can't just add anything.  
-The Redbook will always be "behind" because regulation needs reasonable scientific consensus to sustain any regulatory standard. The Redbook is not a big problem as it deals with methods to obtain reliable scientific data for regulation. The problems are with the interpretation and application of the data.  
- The Redbook provides sound, substantial, validated testing methods. New methods are not validated, not sure what appropriate utilization is, so cannot recommend them. Therefore, Redbook is behind vs. new methodology.  
-Manufacturers want recommendations that they can rely on, perform, and that they can count on FDA accepting the resulting data. Science from the regulator's viewpoint is different from basic science. It's applied science, and the data result must be useful and as determinative as possible in helping to do the assessment.  
-It already has the traditional studies that are needed. Not sure about the regulatory aspects and how to incorporate advances but indicate that they are corroborative and do not replace the traditional studies. New methods might be included as additional tools. Animal studies cannot be totally replaced.  
-The Red Book is disappointing. It is a work in progress; partially done & small part updated over years. Not as useful as it used to be. Therefore, it's relevance is minimized. Reviewers are using other guidance: OECD, EPA, JECFA guidelines. Need more dedicated staff to make it relevant. Can't keep up.  
-Pay attention to what is happening in research. If it is any better (i.e., more sensitive, more accurate, less manpower) then have to validate. Also, we need to look at international harmonization with European countries and other regulatory bodies in the world.  
-It would help if the Redbook committee met regularly and actually acted on any of the presentations that have been given to them in the past regarding new developments in the science. It would help if someone more dynamic would head the committee and there were firm deadlines for revising this guidance.  
- With our current system we can't. Sat on a Redbook committee a few years ago updating the carcinogenicity guidance. It took us 2 years to get comfortable with the changes. The only way we could implement the guidance

was that it was considered Level 2 guidance rather than Level 1 guidance. If it were considered Level 1 guidance we would probably still be trying to implement these changes.

████████:

Update to be current with Tox21, then update accordingly. The classic methods are no longer effective. Need to get to the mechanism of toxicity.

████:

-There have been and will be adjustments and additions to Redbook 2000 to account for concerns with chemicals and potential immunotoxicity, neurotoxicity, carcinogenicity, and developmental and reproductive toxicity (DART). This document is a dynamic progressing document, constantly being updated, and is being referenced to.

-Personally was involved with the Redbook on many levels; I was a member of the upgrade in 2007 and I'm currently the chair to the immunotox upgrade. I do not know and do not understand why there is a lengthy guidance procedure. There should be some revisiting with the lawyers of what was the ultimate purpose of things like the Redbook are. So we slave for years on these guidances and these guidances get stuck (b) (5) █████ and when the guidance does come out its outdated. It doesn't make for good working morale and doesn't make for good guidance.

████:

Need to have expertise in all areas of Redbook; get people to meetings. Get people into both Program and █████ Offices.

-Need to get people to meetings (national and international) because the world is moving toward harmonization. Need to have contact with key players in other agencies.

Redbook contains classic feeding studies for evaluating toxicity using rodents and non-rodents. There are no recommendations for toxicity screening using bio-markers or genome sequencing data, no translational biomarkers (gene alternatives, protein expression), no DNA, RNA, or cancer mentioned, no indication of where high through put assays might be used to for or supplement a lengthy feeding or reproductive study. Our guidance needs to be modernized.

-The Redbook revisions started in the early 90's and is still a work in progress. Will really have to get sensitive to these newer assays (*in vitro* assays). This has been one shortcoming. Our Center has not really put much credence in these assays or much effort to see them incorporate into risk assessment paradigm. Although in fairness they are moving in the right direction. █████ (lead toxicologist) and TOX 21 are moving forward.

-You need to look at hormonal changes and other endpoints. Currently the Redbook looks at morphological changes in tissues. There are changes in glucose, insulin, and kidney function. None of these things were looked at.

████:

Some chapters need updating (e.g., clinical studies)

-Redbook is good for chemicals, but now a typical ingredient is not a chemical.

-The agency has updated its approach, but Redbook is not up-to-date.

-We may get data produced from testing that is not/cannot be required in Redbook, but we need to evaluate these data as well, So Redbook should be updated to include this type of test.

-Driven by █████. Need to update for food additives, but also for dietary supplements. Getting involvement from other offices can be difficult

████:

Should not be keeping it up to date. - █████ dropped Redbook 10 years ago for VICH, which looks to OECD for guidance. Redbook should not be reinventing the wheel; the difficulty in maintaining it emphasizes the problems.

████ dropped the Redbook after became involved with VICH international harmonization; this makes them more aligned with CDER guidelines, but the way they approach the question is still more similar to foods.

-Not used. Have their own VICH guidance. Harmonized with EU and Japan. Refers to OECD for many protocols: different guideline for each toxic endpoint. Keep up-to-date. If revisions are needed (e.g., genotox), then they update.

-Guidance must be consistent, tested, and established. There is a built-in rigidity. Need consensus; thus, it is a time-consuming process. FDA is trying to understand emerging issues as a community of good scientists exercising their judgment, rather than being dogmatic and tied to the language of guidance documents which, even with the best of intentions, don't cover every situation.

-What we have been doing so far is reviewing OECD guidelines. Having inter-agency groups like the Interagency

Coordinating Committee on the Validation of Alternative Methods (ICCVAM) to discuss *in vitro* and other methods that can be used. That probably moves faster than Redbook. It will have to be established every 4 or 5 years, go back to it.

-The guidances we use tell the sponsor the kind of performance we expect from an acceptable method. We don't dictate that you have to do it by specific equipment or whatever. As long as the method meets the levels of performance.

████████:

-The basic principles of the Redbook are fine, but it's going to require a lot of effort to reach some consensus in the scientific community as to what appropriate additions to the Redbook are. And as long as people continue to use the Redbook as a check list of tests that need to be done it will never keep up with the pace of new science.

## Ideas

████████:

-To do this right, need more resources than we have. Requires a significant research investment.

-Keep one person in charge. Their "special topic". Have a set time for review/update (yearly). Talk to everyone involved to see what needs to be updated/changed.

████████:

-Having a dedicated Redbook team would help, but not sure how much. Possibly a mix of senior and junior toxicologists to give the perspective of history vs. comfort with new methods. Interim updates might help, but won't address the problem of updating the document regularly. On the good side, even though not up to date, FDA will accept any data on a case-by-case basis.

-There needs to be willingness to include new information and ideas. The focus on having everything be validated before it can be included may not be the best.

- Need periodic review (3-5 years) to revise/add/drop

-Should be updated every 2 years or so to keep up with changes in methods. Incorporate new test guidelines with global standards. Use of OECD standards and in addition global standards

- Need a task force to regularly update-maybe quarterly, biannually. Especially add in new methods and new review approaches.

-We need more staff if we're going to do that. It's unfortunately nobody's primary job to keep Redbook updated. Everyone agrees that it would be better if Redbook was up to date, but we just don't have the staff to do the things we would like to do.

-We need a dedicated assigned Redbook committee whose task (75% of the time) is revising Redbook, keeping up with what's needed, keeping it current and state of the art. The other 25% of that group's time could help out with the other review tasks. They'd be looking for new scientific methodologies, new scientific tests, validating new study types, recommending to the reviewers new study types. .

-We have to have people that are up on the science. Usually the new hires are fresh out of the labs and know what is coming down the pipe. Constantly revise the Redbook as needed.

- The Redbook needs to be written, but not done in-house. It needs to be done with people in-house guiding experts from the outside. Your experts need to be from a diverse group (physiologists, endocrinologists, true toxicologists, pharmacokineticists, food scientists, nutrition scientists).

████████:

The Redbook Guidance should be regularly reviewed and updated by newly hired reviewers, who will have to review data submitted in conformance with it in decades to come, and by external toxicologists. This will not be done independently; older and more experienced staff people working with them updating and reviewing it. But if we don't have new people look at it, that know things that we don't, it's just going to become more and more solidified. Even internal review by CDER and █████ would be better than no external review. So it's not going to change until someone at a high level in the Agency says this is a priority, it will be updated, and it will get external reviewed.

████████:

-For the Redbook, there should be a standing committee that has some executive type of power. T

████████:

-A working committee consisting of NTP, FDA, and non-department of health and human services food scientists

and clinicians should be formed to come up with methodologies that industry could use for their products. Could lead to faster detection techniques, etc.

- Redbook has not been updated at all. Has to be a concerted effort, with guidance given to keep the Redbook up to date. Serious decision has to be made by management and dedicate manpower. No way to keep pace with science. Not at all a well worked out process. A change in policy needs to be made. No one has taken responsibility. Redbook is stuck in the past and relies on historical data.

-Redbook needs to be reviewed periodically (every 6 months or every year). Should have a committee established to review and update the Redbook. Not sure that this is done. Also, look at literature because we are not the only country looking at these issues (Europe, Japan). Should allow international community if they have used certain valid procedures then we can adapt. If we need the Redbook to be up to date we need to work at it.

[REDACTED]:

One possibility would be to work with industry stakeholders via HESI project committees. This is working well in the genetox arena.

-Another mechanism, or possibly in conjunction with an industry project committee, is better use of the the National Toxicology Program which is supposed to be serving that function. [REDACTED] has said that FDA project nominations focused on validation would be given high priority for funding.

[REDACTED]:

-Need a committee from different offices who have a stake in Redbook and what it has to say. May need to happen at a higher level.

[REDACTED]:

-Don't think that is a viable way to go anymore to update it as a book.

What you need to do is have groups that are assigned with keeping certain subject areas more or less up to date. So if there is a profound change in the way we do carcinogenicity studies that ought to be updated without updating all the other sections. An editor should be assigned to various sections and you need to update it as the science has reached a point of acceptability of rightness to be regulatory science and you have to do it on a scope and scale that is appropriate for the particular section.

-Routine review. The best way for that kind of thing and that includes all guidances and all issues is to have standing committee either within your team or Division. For our group we have two groups: (1) [REDACTED]; and (2) [REDACTED]. So if you have these discussion groups at the Division level that can keep your guidance and other internal guidances relevant rather than going through the Guidance for Industry (GFI). So you can keep things updated on a regular basis.

## 8b. Is there an alternative to the lengthy guidance procedure that you could suggest?

Note that this was answered in several different ways: alternative to Redbook, alternative to procedure for getting guidance approved. ..

[REDACTED]:

At the top, need to push things through quicker (OCC; maybe they need more resources).

[REDACTED]:

- Rather than update the whole thing, just update parts with emerging science (e.g., immunotoxicology guideline, which has been validated by the ICH).

- Possibly provide a short/dry version of the regulations to clarify the requirements for non-industry people or new companies.

We encourage pre-petition consultations to give early guidance. Can tailor the guidelines to the petitioner. Industry has been receptive.

- We need the lengthy guidance procedures for overall safety of our general public. Because of its length it helps prevent a company that is not motivated to get certain compounds from wasting our time.

- Other programs have used a “Decision Tree” approach; it’s a common approach for streamlining.

[REDACTED]:

- Handbook for validated tests for organ systems, rather than self education.

- A cookbook-type protocol could work for some cases.

- Would like to allow some flexibility for toxicology: but industry wants to know exactly what you want.

- It seems that many of the decisions fall to mid-level managers who bring this up to upper management who are busy and don’t want to make changes.

- We have “draft guidance” and the opportunity to publish opinion pieces that can help advance the process, but keep getting bogged down due to other priorities.

- The guidance procedures are in place for good reason, and are not too lengthy--some might say too little. If we need to make changes, we do.

- Shorter guidance may not be feasible from a regulatory standpoint

- Don’t think we can avoid a Redbook. Flowchart giving a summary that refers to the more in-depth guidance.

- Regulatory people to write the guidance, not scientists. Find ways to encourage submission of new/novel data, but not hold results of review against the submitter (e.g., inadequately validated holds up petition or penalizes), so the data could be evaluated over time.

- If CFSAN/[REDACTED] were more involved with internal validation bodies like OECD and could take a broader participation in that, we could lean more heavily on those international organizations and we could feel more confident that there is an OECD protocol that has been validated and accepted for a particular endpoint. We don’t take a very active role in those groups. Rather than start from scratch, these organizations have done a lot of the work. We need to participate in the process so that we can have confidence in their approach or make sure the approach meets the needs.

- Should open the door and ask industry to try to work together to make things more efficient. For new methods we did work with industry because they were the one actually doing it.

- We have had in the past a chapter within Redbook called “Emerging Issues”. Basically it was there to tell the world that we are aware these technologies are there (genomic issues, the genomic revolution, epigenetics, transgenic animals) and the new technologies and science is being done but what goes unspoken is that we are aware of it but it will probably be another 3-4 years before we can actually address them. We do have a system if a company has data that are not addressed in Redbook from a methodology or technique then they may submit this information. If we have the expertise (and sometimes that is the issue too) to review it, we may use these data as supporting data. We actually can incorporate new technologies into our review process, but it’s like “off-label” drug use. We don’t usually get those.

- Keep everything in “draft” form.

[REDACTED] ([REDACTED]):

Tox21 has made this easy: there are screening/battery tests for specific organisms and mechanisms for evaluating one animal vs. many. These methods could save money and still help us hit our target for information.

- Depends on the philosophy behind the testing. We need to resolve this issue before we change our guidance. Need to evaluate potential gains and losses.

- Redbook has had an Emerging Trends chapter at various points. Even to do this, we would need a more concentrated effort. EPA will subcontract this type of work to outside group for recommendations; FDA has to do this with the people who are part of the review process.

████████: Supported science-based evaluation within individual reviews of products or submissions. That would include multiple levels of concurrence for new areas of science but it would allow immediate application.

-Our alternative is the informal case-by-case safety evaluation. We are currently revising our method of exposure assessments to include different age groups (infants, children, adolescents, and pregnant women). We currently will do the exposure assessments for these groups if we think these particular groups would have an exposure to these food contact substances. That is done case-by-case. These are current issues and eventually there may be formal guidance.

████████: -Prefer the Redbook guidance and more, rather than less, specifics for consistency in data submission and continuity as we change personnel. It seems that other regulatory agencies are going away from specific requirements and going towards more ambiguous requirements that they don't state.

-Like to think there would be some kind of flowchart. Think we did do a flowchart when it was updated in 1993. There is no reason why we couldn't develop some sort of program that would help someone trying to decide what experiments to do. To help them make decisions, instead of reading a whole massive guidance document and trying to understand all the intricacies of the guidance document.

████████: No. The established guidelines are good, proven, and conservative.

████████: -Look historically at guidances. What can be communicated through white papers? Until then implementation is not going to happen.

-Have an open forum or the ability to post or blog on the Internet, and put notes down that respond to individual sections. Allow the public (like a Wiki for the Redbook) to rewrite a section, as a suggestion or proposal based on science. The people that respond on that level would be parties that are engaged in science. Could put out calls to scientists for suggestions. Put this out as a blog and link it to the sections of your guidance that needs updating or opening up for discussion. Would need citations. This would automatically post to the Federal Register when you're ready, when you've collected the comments you want to collect.

████████: -Publication on the FDA website, in a peer reviewed journal, or as an OECD test guideline could take the place of level 1 guidance. The OECD test guideline program is becoming increasingly active although (b) (5) ██████████ and the slowness of the procedure make it less attractive. However, because of treaty obligations for mutual acceptance of data, in the absence of guidance there may be pressure to conform to guidelines whether FDA helps write them or not.

-We are thinking of having something (b) (5) ██████████ . We are coming up with a short manual (b) (5) ██████████

-Our group use the procedures of the field itself, like what EPA and ATSDR does. We have different regulatory needs.

████████: Guidance is non-binding, so why does it need to be so specific?

-It would be nice to streamline the process. For example with EFSA, science moves ahead, and then policy reacts.

████████: -████████ uses guidances. The problem is that it is a lengthy procedure with no good alternatives. When a drug is approved, they publish an FOI summary, which includes the method used for risk assessment. So, rather than publish new guidance on risk assessment, a sponsor can see what someone else did to get approval. This is a good way of showing different, current options that were used successfully. It doesn't necessarily include specific methods, but does identify what was important in the risk assessment.

-There needs to be a faster way to develop guidance. One problem is that they seem to need to consult with everyone to make a decision. Slows down the process. Guidance is not law, is not set in stone.

-Difficult to get guidance past the lawyers. Legal holds things up for issues that are not legal. When guidance comes out, it may be behind the science.

-The interesting areas are things that you haven't written guidance for. You could have a "Points to Consider" document that is not guidance but you can update as the teams that are involved in reviewing these types of documents evolve their thinking. This is not a guidance document *per se*, but is something in flux.

-The guidances should be written more generally and focus on the information that you need. From a residue standpoint guidances may say stuff like: We know when you give a drug all the places it could go in an animal body. One of the ways you could do this is conduct this kind of study and give them a high level description of one kind of study. But every single section would finish off, to the extent of which it applies, with something that says: "For alternative study designs and information sources that may be applicable to your product, come and talk to CVM."

- For that kind of coordination they need resources. If it were formalized there would be official resources to fund it. There is an internal document that is used to facilitate reviews. What kind of question to be asked if it is not supplied. How to treat certain types of data. The only problem is that it is internal so it should not be released to industry. It is incumbent on the reviewer to tell them X, Y, and Z. Trying to do a GFI takes 2-3 years to get through (b) (5) it's absurd.

[redacted]:

Get (b) (5) out of it. Guidances are supposed to be issued rapidly.

### **Delaney Clause**

One current limitation or shortcoming is the Delaney Clause (“induced cancer when ingested by man or animal”) and any recognition of secondary mechanisms of carcinogenicity and relevance to man when cancer is induced in the animal model, but only one organ, one species, and one sex. The scientific community talks about that there is clearly a secondary mode of action for this compounds cancer causing effect. As scientists we are reviewing this now and recognize that we understand so much more about cancer than we did in the 1950’s. Currently struggling with trying to see what makes scientific sense on one hand and what complies with the law on the other. Is there something that needs to be done in between to fix that?

EPA (with pesticides) can regulate with a scientific understanding of carcinogenicity mechanism, not FDA – CFSAN – [REDACTED] is now reviewing the current science (b) (5) [REDACTED] and exploring the regulatory language latitude. Is there a way to make Delaney Clause more workable? To allow safe additives in the market place but also protect the public from something that does induce cancer.

Feels that the Delaney Clause is a good clause but you are always going to run into exceptions to the rule. How do you deal with the exceptions?

## 9. How can CFSAN/CVM/OF be more proactive in identifying compounds or issues of emerging safety concern (for example, contaminants, endocrine disruptors, dietary ingredients in conventional food)?

### Commercial DBs

████████: -QSARs can be really good but you don't know if it will become an issue or not; need more resources dedicated to that function.

████████: Ongoing access to commercial databases identifying what ingredients are being added to food.

### Post-market

████████: -Institute systematic cyclic review of previously approved or notified products. In this way we can incorporate emerging science into the system. Now this is done "randomly". New technology can't replace animal studies, but can be good at picking up one thing. They may help to prioritize issues, and then we can do further testing

████████: -Be more aggressive in testing consumer products on the shelf: ~<10% have the content that they say. This would greatly reduce the amount of adulteration

-Our division is being proactive: have identified some compounds that are on the market (e.g., melatonin, which was reviewed as a dietary supplement, but was not approved for use in foods) that are already in foods. Check products on the market (consumer safety officers), check the literature.

-Allocate specific resources for post-market work, not just pre-market: First explore the differences between the two (e.g., larger burden for post vs. pre; more leverage for pre- vs. post). Sometimes problems are identified but the enforcement/compliance is not consistent with risk assessment part of the review. Lawyers are reluctant to take action except in serious situations (contrast lack of data vs. actual harm). Re-examine cyclic review of food ingredients: is it of value or not?

████████: -Suggests that the scientists receive updates via email from person that has received adverse reports. Someone should be in charge of the adverse reports and create a table of the adverse reports. There is supposed to be a database of adverse reports and we were told that we could call them. But would like a summary of the complaints that is sent out internally once a month.

████████: -We don't go back and do any post-market analysis after approval, additive-wise. That could be a chemical safety issue, that things are being just approved. There is no step like every 5 years recheck on something like EPA does. There has been a discussion of doing this but it comes down to a matter of resources. But if you had the programming mathematical computational program it would be a matter of rerunning the program every 5 years with the data inputs.

████████: Need to promote CAERS (CFSAN Adverse Event Reporting System): people need to know where to report problems.

-Need to put the message out that this is available. We do not do a good job with this. Could improve web-site.

-Because we don't require human data before a substance goes out, the human data is people being exposed post-market.

-Our post-market surveillance is consumers voicing their opinions.

We should establish "active surveillance" the first year or two a product is on the market.

████████: -FDA has a program for recording any reported adverse effects. Should take action to immediately collect more data on these.

### Outreach

[REDACTED]:

Keep up with industry. Go to scientific meetings (now 1/yr). Talking with and developing issues with industry: - networking and intelligence. Usually there is not enough money for trade meetings. Review literature, including trade literature. Moffett is a good asset because provides an interface with industry.

-Ensure that there are good bridges between FDA, industry, and trade associations. Try to work more closely with them because they are on top of literature as well and looking for problems. So attending conferences and trade associations; having memorandum of understanding (MOU) and confidentiality agreements between some of these groups so that they are comfortable telling us they have an issue with this. Some people are a little cagey about telling the FDA because they could be act upon by legal processes. Strengthen that collaboration or alleviate those concerns so they're more forthcoming. The food industry is working more towards that, wanting to be more transparent, and want to share data.

[REDACTED]:

-If the Agency was more proactive in being a presence at food manufacturing conferences we would be more aware of what is coming down the pipe and would be able to address questions.

[REDACTED]:

Typically not proactive, mostly reactive. It is hard to predict emerging safety concerns. Some things never go away/always come back. Send more people, maybe expert panels, out there with industry (e.g., ingredients suppliers) to get exposure to new techniques, ingredients, supplements. Need more "intel" to get a heads up on what is coming into the market.

-People with outside experience of FDA might help because they deal with these issues on a daily basis. If asked to participate they will.

[REDACTED]:

[REDACTED] has instituted programs to be proactive with industry.

-Encourage them to work with us prior to submitting data. Asked for quarterly "portfolio" meetings. Can talk about what's in-house and what's coming up. Can set up seminars, meetings with IVET group (group discussing innovation)

-Have established "tech teams" to go across the Center and work with industry on new technology.

-This has enabled a 12- to 18-month timeframe: reach a consensus and understanding on technology, identify the risk questions, put together the high level questions sufficient with the technology, and work with product so that you can hand off to review team. Can shape questions and data requirements. When the firm comes in with the new product, you can give them this information and put them on a program path for review that is consistent with a more traditional approach.

-Being in touch with consumers, stakeholders, drug sponsors, universities. They may come across something new first. If we are aware, we can plan ahead.

[REDACTED]:

We could work together with industry and academic groups to try to come up with a paradigm for ways that one could identify the next "boogey man" coming down the street. In developing methods to try to find out ways to determine whether something could be a problem not whether compound X is a problem.

## Mtgs/confs/journals

[REDACTED]:

-By paying more attention to the literature/attending more conferences. Now you have to be presenting or invited to attend meetings; training money is limited to local travel. Need to make the travel process less burdensome (less paperwork and clearance)

-Maintain our funding to allow scientists to go to conferences.

-By sending the scientists to more conferences. We get a lot of training money which is great to understand new procedures and new methods. But not sure if there is separate money for conferences. Just to see what research is being done out there and what people are investigating.

-Recently were told that our access to scientific journals have been taken away because of budget restraints. We have to be proactive as researchers and read up on what is happening in the real world and the world of science. Networking helps a lot, meeting scientists at universities that do this kind of work and bringing those researcher into our facilities to discuss what they are doing on a real time basis would be proactive in nature.

[REDACTED]:

-Conference participation. Be more active in the scientific community. Active, publishing, giving talks will keep current.

-Some individuals trying to devise a text -mining effort  
--Journals/workshops/conferences. Online classes, webinars, webcasts to save travel money. Academia. Important to have access.

████████:

-First must do a literature search to see what has been done. What compounds are potential health hazards?  
-Our group is proactive in a way by publishing manuscripts and getting them peer reviewed so they get feedback. Participating in meetings and panels and other areas that do address these issues. We need to maintain that but will run into trouble this coming year as the budget constraints may limit people's ability to participate in the outside community.

████████:

-Educate scientists: need to go to be meetings to be exposed to the most up-to-date information; otherwise, will lose touch.  
-You need to listen to the science, read as much as you can, go to meetings where they are discussing evolving new science, and constantly think about how it will impact the work I do.

### **Internal comm.**

████████:

-Integrating disciplines is a way of being proactive: utilizing existing knowledge from different areas allows you to view whole food mixture rather than a single compound, maximum dose.  
-Improve communication and collaboration and willingness to consider new approaches.  
-The scientists from CFSAN and █████ have to talk to one another.

████████:

We are doing a pretty good job, but could get research scientists more connected with Program Offices. Some mechanism for people to talk, rank issues. Would need oversight to set the priorities  
-More communication between program and research offices. Things are improving, but people in the other offices have no idea what is done in research and vice-versa.  
-In the past, issues may have been identified as important early at the research level, but were not supported by the other offices until they became an issue.

████████:

Collaborate/interact more. Designate a committee for these issues.  
-Allow people to stay up-to-date. Tend to get hung up on day-to-day drug review. Need to allot time for this, create more focus groups (not just in response to something that comes in), even small ones, to get started, so that we're ready when something new comes in.  
-Can participate in working groups to address new issues (nanotech) before products come in.  
-Maybe we need a way to let scientists share information or concerns. A type of internal forum where the reviewers and the risk managers could get together and just talk about issues of concern without bringing it to a manager, setting it on the desk, and saying now do something about this. How do we get the managers to listen to the scientists who have information on what these issues are going to be about?  
-Letting the staff get training and attend meetings.  
-At some level within the Division, regular meetings of chemists and regular meetings of the toxicologists. Also regular group meetings if someone finds something, is interest in something, or something is in the literature that they routinely research; and should presented it to the group for an opinion as to what we should be doing about it. Maybe doing a memorandum of understanding (MOU) with █████ in order to do some sampling. For █████ that is traditional.

████████:

-Emphasized the importance of the "listening post" for emerging issues so that these are put on the radar and move forward. Scientists need to feel they have informed and were heard. Felt █████, past █████ of █████, was the best because he listened. Office level below dealing with different issues, limited resources, how to maintain the "squeaky wheel", ways to retain talent.

### **Dedicated staff**

████████:

-Dedicated person/group for post-market issues.

-One chemist/toxicologist whose job it is to stay on top of research literature to see what is being done (e.g., read journals). This does not have to be limited to supervisors. In addition, information from meetings/conferences could be provided to this person.

████████: Perhaps an ombudsman or an increase in HPO (high performing organization) efforts which can encourage bringing issues out early, ability to discuss within discipline-centered groups (and across groups), and other open discussions as we see things that potentially could be problems.

-Dedicated staff for routine marketing, especially post-market issues.

-Establish a group that tries to keep an eye on emerging threats (watch EFSA, other agencies).

-Cyclic literature review. The need a standing Ad hoc committee. For every safety review of submission that we do the toxicologist has to review all of the data for each exposure we are evaluating. If a toxicologist identifies a significant new safety issue, that toxicologist must forward the information and alert the supervisor, but management cannot just drop the ball. They have to say okay this looks like it may be an issue and inform a committee to deal with it or make sure it is routed somewhere so that particular issue is addressed and not just dropped (e.g., new toxicity equivalent factor (TEF) for dioxins and carcinogenicity study for dioxins-(b) (5)).

████████: -A designated person that monitors anything that comes out on any topic all the time. Someone on a regular basis scans the blogs, the communications, the whatever, and then they filter out by pattern recognition what is a potential emerging issue. People that monitor the lay of the land before things happen. Look for spikes, look for red flags that come up.

████████: There definitely needs to be a central location (an office or FTE) that just gathers this information. Right now it is done on a case-by-case basis. But if there was some central location that was keeping track of this and the statistics from academia, the public, and the media, that would be better than case-by-case that our projects work with.

████████: -We need to have a small group (1-2 people) whose job it is to look for issues of emerging safety concerns, but also the commitment to use the information they collect. Make it somebody's job to look for those things. There is some effort to look at pathogens and we need to do something similar with chemicals and things like that.

████████: -May form workgroups and assign more work, but upper management needs to decide. Some scientists with 20 or more years of experience feel that they are under-used and need more responsibility. System should make the best use.

-This needs to be done by committee. It will not get resolved until you have a multi-pronged approach to it.

████████: This is mostly a resource issue. To get out of reactive mode we could compile some sort of master plan, but unless the Foods Program is committed to diverting resources from elsewhere there will be no way to implement a plan to do something proactive about contaminants or endocrine disruptors. This is particularly true of self-affirmed GRAS/dietary ingredients although there are extra layers of policy issues surrounding that which are probably at least as important as the safety issues themselves.

████████: -Have to devote resources to putting a group together to do that. There needs to be a concerted effort to identify emerging issues. It has to be across Centers including Office of █████ and █████. It takes time to do signal detection and data mining that is necessary to do that. We are still very much in a reactive mode on that kind of stuff. Have to look at everything. The data mining has to include adverse events, reporting the reportable food registry, have to have some connections to the States. These are all valuable data sources that need to be integrated somehow.

## Watch list

-Each program and research office should submit a Top 5 chemicals of concern. The Center leadership could combine and identify a Top 20. Need to set a time limit and make it a high priority; make it a deliverable, tie it into each person's review

-CDER has established a list of compounds to watch for carcinogens, but what about liver, kidney, etc?

████████: -We proposed the "Watch List" or some facsimile to prioritize issues that are likely to present safety issues and have

them monitored as a routine practice to restore confidence in the agency's commitment to public health, particularly for post-market issues, but also for anticipated new contaminants and dietary ingredients.

-Have proposed a "Watch List" of potential problems like BPA (b) (5)

This was sent out to offices to ask for suggestions for chemicals like this to put on the list. They recommended using interns and one toxicologist to monitor these chemicals. Management stopped supporting this idea.

-Several years ago, two of our senior scientists within the Center had created a "watch list", looking for volunteers to take compounds or recommend compounds for this "watch list". In theory they would follow-up maybe once per month and check the literature to see what is being written. Usually these compounds are already approved food additives or color additives or food contact substances. In the past two years, this "watch list" is starting to get active again. The name has been changed to the "alert list". We are trying to develop methodologies for assessing this. Just yesterday we had it added to our research gaps needs. We are looking at things such as social data mining. We are trying to develop a hierarchy on what type of information we'd use for this "alert list". Publications are probably the top priority, any news releases would be another priority to get a feel for what may be happening with the compounds that are out there.

\_\_\_\_\_:

-Allowing the reviewers or review teams to submit chemicals of interest and have the Science Policy Office coordinate a list of such chemicals and identify similar emerging issues or concerns that could be addressed.

## Other

-Individual scientists need to stay current; reward those who go above and beyond in this area; recognition would provide incentive.

-Some of these are not new (e.g., endocrine disruptors, Vitamin D). Need to consider applying existing data to "new issues" to be proactive in other areas

-In terms of premarket approval, that's not our job. We have become reactionary. Being proactive is not our mandate. Do we have funding to look at these things? If you want to be proactive, watch what Oprah or what the newspaper is talking about today, and that's what our issue will be tomorrow, regardless of whether or not it's based on science.

-It appears that we are all reactive. Limited by resources. Also, nature of the issue: would not expect to be proactive in identifying contaminants--you might not expect to find certain compounds in foods. Do keep up with the science of known chemical contaminants (e.g., metals); pesticide program pretty weak.

-At least prioritize the issues

-Need to get more information based on market data, rather than relying on the stated amounts of ingredients in products. Need to develop a database for dietary supplements to help evaluate potential intake, which can vary widely from person to person.

- Need to have a proactive response to new scientific findings (published) indicating potential risk from a food or food contact product before they get to be a big issue. It's possible BPA could have been headed off if FDA had stepped in earlier and addressed the old in vitro data that had come up.

-There is not a great need to be more proactive. Consumer protection agencies are very proactive and make sure we're aware of potential issues. Maybe industry could provide more voluntary updates (e.g., identify abandoned uses). Public may be concerned about something that isn't used in the market much.

\_\_\_\_\_:

-We should be especially aware of what other Agencies spending resources on (e.g., EPA Risk Assessment Forum, EPA Risk Assessment Guidance and Tools, EFSA Scientific Opinions and Guidance, NTP Report on Carcinogens etc.) that can raise questions on our focus on safety to even previously approved chemicals.

\_\_\_\_\_:

-If we can do an SAR that helps to identify compounds that could be bad actors. That's how we are proactive in keeping genotoxic compounds out of the food supply and so maybe we could do it with the endocrine disruptors.

\_\_\_\_\_:

-Don't think the issue is identifying compounds or issues, but making sure they don't get buried in the wash of priorities.

\_\_\_\_\_:

-If they did have this cumulative exposure from all sources. If we monitored the cumulative exposure then we would be able to see if something is used more than we anticipated. If the exposure is changing then it would be an

obvious trigger. Maybe if we had a dedicated group of people responsible for monitoring the press (large, small, and outlets) and identify trends.

[REDACTED]:

- Need a system where there is objective oversight; better way to fish out good data.
- Difficult to go out and look for good data because we're defensive.
- -NCS (National Children's Study) is a good source of better data. We should be involved in this as a center.
- Even more consumer data would be good: surveys, focus groups.

[REDACTED]:

- Follow what chemical products are approved for use in outside countries from which we import food and drugs.
- Pay attention to influencing factors (like weather for mycotoxins in grains)
- We do pretty well: we are aligning with Tox21. We stay on top of current developments in toxicology. This is the best way to be proactive.
- Make a web-site to solicit public comments. Would need more people or a group to focus on this--things like inspections, border control, expand the percentage of foods that we are monitoring.
- So in terms of identifying we are aware, but in terms of doing something I don't know it is part of the scope and mission.

## 10a. What internal processes are in place to ensure appropriate quality assurance and peer review on chemical safety matters?

### Research

████████: -Research has a QA program with inspections, etc.  
-Not aware of any internal processes in place for peer review in chemical safety matters; however, they may be used in a particular office that he is not aware of. As for QA, not sure there is any beyond the team members assembling a given assessment.  
-There is an active QA program. Every six months the labs, notebooks, and records are checked. Assumes this is true for all Centers. This works well. Check labs, SOPs and safety suits are checked.

████████: QA procedures in the labs have been a problem in the Center. We make industry go through an incredible process with GLP, but we ourselves are sloppy to adhering to it. Don't think that those processes are well established. The QA is a "step child". They could never find enough people to do it. There is so much a sense of ownership of their books and their research, and feel that they should not be questioned. The attitude in the Center is individuated rather than a common goal. An SOP is the way to do it so they know what is expected, what the procedures are, and what to do if there is a problem to document.

### Petition review

Good process in place; good communication.

████████: -Was able to get a meeting with a different office to fill in gaps for a compound without much exposure data. They were able to provide some additional exposure information. If we need help, we can contact them. As to whether it is effective, it depends on their response.  
-Try to stick to the lowest level needed.  
-External issues: people attend JECFA and Codex meetings (FA has a team in place for clearance/issues and contacts the appropriate people)

████████: -For internal memos, supervisor is first line of QA; for larger issues, higher levels of management. Normally this is sufficient (9 times out of 10 OK).  
For regulatory scientists, there is a questionable peer review process. For big petitions, different studies are done by different scientists working independently. They are not encouraged to communicate with each other in such a way as to improve quality of the review. There is a lack of exchange even between toxicologists, which can reduce the quality of the review.  
-Not enough, but we have two interdisciplinary standing committees, the Cancer Assessment Committee and the Quantitative Risk Assessment Committees to perform reliable internal assessments. But, these only deal with carcinogens. These provide a reliable internal gauge vs. the Delaney Clause.

### Notifications

████████: Internal administrative reviews. No reviewer is unilateral. Each is vetted by at least one supervisor; for controversial issues, more than one supervisor. Can convene a board of experts (senior scientists within the office) for high levels. And coordinate at a higher level as needed (e.g., for an issue like BPA)--division directors. SOPs in place. There is a formal procedure for resolution of scientific disputes if needed. Chemistry issues open to less interpretation than tox issues.  
-QA is internal within the division goes from reviewer through supervisor/division head. Things are rarely sent out for peer review.

████████: It (GRAS Notification process) is always a group decision, not an individual decision. They deliberate and challenge each other. If you have a strong view, need to be able to defend it with data and evidence.  
-May go to an outside expert committee in some cases.

- The established chain of command is our QC. In addition to which, the information that we look at has been recognized in the science community (including WHO, JECFA, EFSA) based on its having been published.
- Each action is looked at by three major groups: chemistry, toxicology, environmental. There is an initial meeting to evaluate the submission.

[REDACTED]

No SOP for review and compilation of contaminants data generated through the compliance program.

- No cross-check of any data that are compiled; written by one person and sent out. Same for exposure/consumption estimates. No one checks.
- Some safety assessments are prepared by one person and reviewed by the [REDACTED]
- Once work leaves an office or group, is assumed to be correct.
- The work is done quickly; has seen mistakes. Nos. may be correct in report, but used incorrectly in memo.
- Have to follow specific guideline requirements for each chemical. Feels there is no oversight on decisions.
- Some of the major risk assessments have been subject to peer review. Other than that, it is not clear that there is a formal mechanism for peer review.

## Other

[REDACTED]:

-Not many. Often the conclusions of a single reviewer drive a safety assessment. Even if a supervisor reviews, he is unlikely to go in-depth. Only big problems get big involvement. Something new (e.g., Olestra) does get a higher level of review such as a Scientific Advisory Board hearing, but it's difficult to get participants, and a lengthy process.

[REDACTED]:

Not. Within an office there are procedures: a review moves through various levels.

-But for inter-Agency documents and when there are disagreements, there is no process in place: goes to the [REDACTED]s, and the scientists are left out.

[REDACTED]:

-First line scientific management is generally the only check on safety review work. While the Food Additive Petition process allows time for peer interaction and voluntary peer review, the Notification processes (Food Contact and GRAS) generally do not provide sufficient time or encourage peer interaction.

[REDACTED]:

No peer review in cosmetics. Reviewed within Office. For toxicology/pharmacology review, it is helpful if a senior level reviews junior level review, but not happening now. Don't have any processes. Do not have an SOP on how to review chemicals in [REDACTED]. This would be helpful.

[REDACTED]:

-Traditional: there is a review team, team leader, division director. Past that it is difficult to balance a transparent peer review process against a timely and a proprietary review. There is a QA and QC program that evaluates end-product (letters to industry), but peer review oversight is at a lower level: they encourage team level discussions, but this is not required and can't be done for everyone.

-Involvement with global organizations may allow some peer review. -There isn't really a residue chemists' group.

-We have SOPs, P&Ps, and guidance to follow when doing a review. The review can either go to peers or the team leader, and then to the division director.

## 10b. How well are we implementing these processes?

[REDACTED]:

Not sure how formal the process is. Seem to do well on the big issue

-We do a pretty good job in [REDACTED]. Sometimes documents from other offices are finalized before we see a draft in [REDACTED], and this can be too late for review. There is usually higher level down communication on big issues, but sometimes things are missed.

[REDACTED]:

The two Chemistry supervisors often have differencing views and there is no one available to resolve these.

-Often, other reviewers (Tox or Chem) are not aware of the issues because we work in silos.

-This is implemented well. The supervisor take their role of signing-off memos seriously. It's not a rubber stamp; they do read and provide comments.

-Some of it is the individual toxicologists dropping the ball. They don't do a thorough review of the record or the literature and they miss stuff. But when there is an alert in a memorandum is must be followed-through. Once a problem is noted and it's on upper management's radar then there is good follow-through. But the problem is getting it on the upper management's radar.

[REDACTED]:

It is a small group and growing smaller; the number of employees is not adequate to cover the issues coming to us. This year they have new supervisors (detailees). The reviewers feel they are short of guidance because the supervisors don't have specific knowledge or the expertise to confirm that their work is accurate.

-If we were doing a crappy job regulated industry would be jumping up and down. In my experience with the pre-market review programs, the majority of submitters understands and supports the safety reviews, even when they get "bad day" responses.

[REDACTED]:

Well

[REDACTED] [REDACTED]:

Don't know how well we do on peer review. Don't think we do a very good job making sure we are consistent with how we decided things in the past. When someone leaves there goes the past. We need a system in place so that we can document how we made the decisions and why we made the decisions. ONADE has done well in having quality assurance and having SOPs, but on our decision-making we don't have a consistent approach. Perhaps we need SOPs or something to say these are the factors that went into making the decision using the chemical safety review information. Get the science right but sometimes there are some non-science issues that affect the final decision.

## 10c. What additional processes, if any, do you recommend?

### Formal process/SOPs

Need to have QA in general processes, not just by study but as a big picture approach/process.

[REDACTED]:

We need to invigorate our CFSAN Bioresearch Monitoring Program. FDA has an Agency-mandated Bioresearch Monitoring Program and respectively each Center has a program. The other centers ([REDACTED] and [REDACTED]) have their own programs. The program shows that there is data integrity, quality assurance, and the studies are used to support safety of products that the various Centers regulated. The CFSAN program is small and very inactive at this point and it needs to be revamped and expanded. We have considered running a joint Bioresearch Monitoring Program with [REDACTED] and CFSAN.

[REDACTED]:

Need SOPs and cross-checking. More checks and balances, just to catch errors.

-Whatever is publicized or posted must be accurate, and we should be very careful about it.

-More than just one person doing a given job. Experts, plus someone not directly involved in the project, but who knows what to look for.

-Improve consistencies across the offices.

[REDACTED]:

-Develop a committee within FDA that deals with inter-office disputes. Needs to be science, not lawyer-oriented. Needs to be internal vs. the peer review process, which is external.

-We don't value our own opinion here.

-Top positions aren't scientists.

-Medical officers are not used as much as they should be (due to territoriality)

[REDACTED]:

-Regular meetings with industry for feedback. Both sides can point out problems. Reevaluating QC program to improve implementation.

-Science quality can be lost if you pay too much attention to the template. It is most important that the review be clear and logical.

### O/S or subject experts

[REDACTED]:

Used to have a focal point expert, "head chemist" who could look over everything and had a lot of experience.

-Need a system within the office to make it easier to identify/contact the correct person. Now they go through the CSO to get to the correct person.

[REDACTED]:

-For some issues, a subject matter expert would be better [than the established tiered review process].

-We certainly could use more experienced, senior expertise in the office.

-Handy access to experts in various fields for answering questions quickly.

[REDACTED] ([REDACTED]):

Could use an external food advisory panel to vet FDA conclusions; however, this would be expensive.

[REDACTED]:

-Within the specialized groups, allow more dedication to specific topics. Usually it's a group of people doing multiple jobs.

[REDACTED]:

-Should be peer reviewed from my peers not from the people that are supervisors or let editors of the journals sort it out.

[REDACTED]:

-Would recommend wider use of the CAC for all concern level III food additives and any constituents reported to increase cancer in an appropriate animal model: committee is cross-discipline and includes pathologists, biostatisticians, epidemiologists, chemists, toxicologists, and consumer safety officers. Also, if there is not a consensus on the CAC or if management had some issue there could be some kind of outside process, whether it be with OF, [REDACTED], or even outside the Agency.

### Post/publish reviews

████████: -Any post-market review should be published; they are transparent, based on literature; we should be able to stand behind them

████████: Internal peer review panel could look at, comment, and revise assessments. A way to post chemical safety reviews on the website, where others could review and comment. Not sure something like this is in place or not. -More input early on would improve assessments. Consider Six Sigma Design of Experiments to help develop a process to improve the quality of risk assessments.

## Exchange reviews

████████: -More QA is needed. If one team leader can't review, or even if they have, it would be good for the second team leader to look over, even if only the conclusions. Tox reviewers rely on chemistry who does the first review to determine exposure. If their exposure calculation turns out to be wrong or needs to be changed, then toxicology needs to redo their assessment. Should achieve consensus on the two teams before moving through.

- To maintain consistency, more QA review by the managers is needed (e.g., two toxicology leaders would assess conclusions from both groups). In other words, a submission from one line should be looked at by managers of both teams to achieve a consensus before it goes to the next step. Would like to have second eye on what she does to catch small mistakes. A lot more editing needs to be done. There should be another level of critical review.

## Peer review

████████: Institute a separate review team that is charged with secondary review, but they should be outside the office/division director that has done the primary review.

████████: A Center-wide committee to look at the overall decision made by █████ when there is a new entity or substantial questions (e.g., human protein in GRAS). You need experience and preliminary assessment before going further.

-Personally, would require a consult with pathologists in cancer causing agents.

████████: -It's important that if people are going to do some sort of peer review, they actually are reviewed by people who are their peers and they understand the science. My area consistently had an issue with people who didn't know anything about the field who were supposedly peer reviewing and making irrelevant comments because they don't understand the field.

████████: -Need supervisors with better scientific knowledge in their area to review the product. Need someone to provide oversight and critical review

████████: -When letters go out it important to have "new eyes". It can be a CSO or someone with experience checking details (i.e., name, company, number of pages); QA by CSO to look at it for minor mistakes/details.

-I might suggest something that I **don't** like because for reasons is that it becomes misused, is to ask someone else to look at what I wrote and ask questions. If it is done up front and at a peer level it would not be so bad. Leave it up to the primary reviewer to select someone.

████████: -We need to subject our work to more internal peer review from outside our own operating units.

## Internal comm.

████████: Communication is key. They don't wait for a formal update meeting to raise issues. Feels that chemists are well placed; very cohesive unit even though they've been broken out. Different culture between chemists vs. toxicologists.

-There are weekly chem meetings to discuss issues across food packaging, additives, GRAS biotech. Believes these are unique to the office. The meetings improve consistency and utilization of methods across groups.

■■■■■:  
-For common compounds (multi-Centered) they should consult with other Centers and Offices and in special cases it should be Agency-wide (e.g., endocrine disruptors merits Agency-wide discussion). CFSAN/■■■■■ may have better ways of dealing with this, to enhance the communication.

■■■■■:  
Communication needs to be improved between offices and labs. Research scientists should be consulted earlier in the review process. -Only occasionally are research scientists asked to look at a review and usually after it has been completed: e.g., for BPA, some early research had been done, but it was not incorporated into the decision.

-Trying to build or enhance communication between Offices and Centers to ensure that the research we're doing is meeting their needs as well.

■■■■■:  
Get more involved with other experts in the agency--CDER, CBER, CFSAN. This is usually restricted to controversial issues. It would be helpful to have at least one contact at every center that we could go to, or to have other centers review risk assessments more routinely.

## Other

-Periodic reconsideration of issues captured by an ombudsman or someone independent could help identify weaknesses and maybe discern solutions in the form of better processes.  
-All other toxicities that potentially impinge on the public health should also have mutual, not segregated, team or committee assessment to ensure reliability. Each assessment now tends to be vertical. "Group think" is needed to avoid mistakes.  
-Problem is more regulatory: once something is in 21 CFR, can't take it out. Notifications can't be withdrawn (e.g., BPA). Maybe the laws should be changed.

■■■■■:  
The processes in place are sufficient. Need to maintain high internal standards. Supervisors are responsible for the proper use of personnel; determine where the work is needed and who best to do it.

-Institute regular 5-year review of chemicals and publish those results. Again, this would provide QA & peer review. Each substance could have its own docket, and a consumer safety officer could be in charge who people could contact.

-We [GRAS] could use a technical editor/journal reviewer to get it ready for the Web. Now the burden is on the memo writer. In addition to their other work duties before they upload it to the Web.

■■■■■:  
-For peer review: some drugs are evaluated here or by the EU, or internationally. We may get pressure from outside to allow import of meat treated with a certain drug approved by EU if JECFA approved. The question comes up of whether we should now approve the drug here automatically or just approve the imported food. In the future this could cause conflicts with our standards.

-We don't have a system to go back and revise or re-evaluate decisions on a 5- or 10-year cycle. Only major issues come back. Once something is approved, it is hard to go back.

-CFSAN has editors (he believes) to go over reviews.

-Her team/division does very well with on-the-job training.

## Communication/Collaboration within OF/CFSAN/CVM/NCTR:

### 1a. How effective is the coordination and collaboration across offices and centers on cross-cutting issues?

\_\_\_\_\_:

At the staff level, there is not much formal collaboration; this is unfortunate.

-One of the best examples was a guy from the research labs did a detail as acting \_\_\_\_\_. He was good and it gave us a good connection with the lab. It helped to establish a good relationship and one that we are continuing to use.

- There is not a lot of it, but when we do, have points of contact within USDA, EPA, CVM, so if there is a cross-cutting issue, we how to get people involved (e.g., USDA on meat and poultry).

- \_\_\_\_\_ maintain a good relationship with the labs. They send representatives to chemistry meetings. Chems would be willing to have the same type of meetings with the regulatory side, but they don't have them. Since lab group was separated from the office it is a little more difficult, but there is still personal communication; no formal collaboration. Has seen more consulting from the regulatory side recently concerning recall issues (e.g., phthalate contamination of beverages). Ad hoc. Team is assembled to address a crisis situation. This seems to work well because now everyone is included.

-Not effective. Very difficult to achieve. Need to find someone at your level if you want to make it easy. It is too much red tape when you have to go through your supervisor. Difficult to find people who are working on the same topics in different groups.

-Between Centers there is not. It is difficult to access information from CDER. It would be nice to have access to each other's data within FDA more easily.

-Only had experienced with \_\_\_\_\_, it's not particularly effective. We are willing to collaborate but no one is willing to give up, so basically two groups are doing the same review. No one is deferring to another Office. As long as both of those groups care about it for different reasons you are getting duplication of effort.

\_\_\_\_\_:

-Not aware of much going on (new employee). People want it, but it doesn't happen.

-At my level, I see very little coordination and collaboration across offices and centers on cross-cutting issues.

-Good within the division.

-Interoffice and intercenter (with the exception of NCTR) communication/collaboration is virtually non-existent.

-There is very little forward-looking that is shared across Centers to identify potential areas of concern; this needs to be done.

- There is good coordination between the DS and FA groups (e.g., macrobiotics); there is good consulting back and forth.

-Sometimes companies get a rejection from CFSAN, then turn around and submit to \_\_\_\_\_. If they communicate, they can catch the double dip. Need an open line.

-Good for both. If we need information, we can get it from another office. Sometimes it is hard to find an expert within the Center. However, sometimes we do not realize that the same substance is being worked on in different groups, even between offices or within a division (e.g., between (b) (5) \_\_\_\_\_). May not find out until it becomes a big issue (e.g., (b) (5) \_\_\_\_\_).

-In the last two years there have been improvements in communication in the different offices CFSAN/\_\_\_\_\_ to solve regulatory issues.

-Depends on the personnel involved: some are open to direct communication (just send an e-mail), others are more straight-laced and must follow a bureaucratic pathway. For external supervision, it depends on the supervisor.

\_\_\_\_\_:

Very good within CFSAN, and excellent between Dietary Supplements and \_\_\_\_\_. Not so good with \_\_\_\_\_.

\_\_\_\_\_:

We don't do the cumulative exposure assessments for chemicals that are regulated by other Centers. We don't have a way to do this.

\_\_\_\_\_:

-Good. CFSAN Pathology performs pathology reviews for CVM (Division of Human Food Safety, Office of New Animal Drug Evaluation) about once per year. NCTR / NTP / TSSRC / CFSAN (and their TPA or NTP pathologists) meet multiple times per year on various issues (furan, BPA, aloe vera, dietary supplements).

-After the reorganization, it is my every day engagement and strive to reach out to strive for collaboration. I collaborate a lot with other Centers because pathology is not well-known. Most Centers don't have pathologists, so

we really reach out to anybody who may need our services. It is my personal effort. If I didn't do that we would just sit there. In our own Center, there is very little outreach across Offices.

[REDACTED]:

It is driven by individual initiative rather than Agency directive. We have very limited communication – only between "friends" or when mandated by crises.

[REDACTED]:

Getting better. The Strategic Plan is bringing researchers and Program Offices together for the first time. Feels that inclusion of scientists in programs in improving over the past.

-There is some across our office and other centers on issues like nanotechnology, but the individual bench scientist isn't always in on the discussion: if a manager wants you to work on a cross-cutting issue, you're told to do it. There are no intellectual contributions from the scientists into research projects: sometimes need to work backwards to make it fit in with foods.

-Yes, collaboration exists across offices and centers on chemical safety issues. Coordination is not well established and is more informal. Sometimes they need to just go and ask. Would be nice to have a process in place to make research offices communicate. There is some collaboration between CFSAN labs and NCTR, with each doing a separate part to resolve an issue

-Becoming very good now, it's person oriented, [REDACTED] helpful. Predecessors ([REDACTED] and even [REDACTED]) were barriers to any cross cutting collaboration. Now actively encouraged to collaborate with USDA, NCTR, and CVM.

-A monthly seminar system is available where scientists from CFSAN and CVM participate and it is open to other scientists via webinar. This has been successful. (b) (5)

-By creating the OF there is enhanced communication and working together, but there is still more that needs to be done.

[REDACTED]:

-There is some collaborating/coordinating within CFSAN and NCTR on some research projects. It has gotten better over time.

[REDACTED]:

There is not much coordination: OFS, Office of Nutrition and Dietary Supplements all do dietary exposure/food consumption estimates; Microbial Risk Assessments group uses the estimates.

-Have tried to get a working group, meet periodically, share expertise, and find out what people are working on, to do things more consistently. But never gets off the ground.

[REDACTED]:

Terrible. Offices work independently; have their own structure.

-Something involving different offices is very difficult to get done; different opinions, different policy decisions; takes longer to settle everyone's fears.

-Office of Communications is taking a proactive approach to getting people involved: "one voice for the Center."

[REDACTED]:

-It is really good when one side reaches out and asks for help (CFSAN, NCTR, CDER, and CBER). Lacking outreach it is poor. Do this more for specific issues and questions and it works well. There is great desire for bettering cross-communication, but a dearth of good answers. Better ideas for cross-training or leveraging training opportunities, but the physical separation is a big barrier.

-Quite effective in some ways. Depends on who you're dealing with and how organized they are and what the goal is.

-Not very. Offices seem to have a "wall" between them--you may feel you're being held up by the other office or vice-versa. There tends to be butting of heads, and lack of communication that make it hard to move on to the science. Strong personalities: "we've been doing this so long; therefore, it must be right." It seems the tension may go back years.

-Works for issues that are applicable to more than one office or center. Need someone at a higher level to identify the issue and initiate the communication.

- Within [REDACTED], it's collegial but not necessarily timely due to sudden emergencies. For the most part, when we get people involved early the interactions are good and things turn out well. Across Centers, we are currently in a bit of a discussion with CFSAN over something they want published that doesn't match up with what we ([REDACTED]) do at all. We are late to the game, they are not taking much mind of our comments or suggestions, and it's just uncomfortable.

- We collaborate with NCTR on several research projects. We go to seminars. We collaborate with the pathologists at CFSAN. They have been a great resource for us because we do not have pathologists on site. I
- One doesn't know enough of what is going on in the other Centers.
- Another example: Acrylamide issue in fried foods was well orchestrated by CFSAN.

[REDACTED] :

Think we have a ways to go. In terms of across Offices it needs more work. Leadership has to pay more attention to that. A lot of times you do your part and this other group does their part. Then somebody makes a decision. Well how did that happen? Everyone was left hanging on how the final decision was made. Sometimes that is lacking. A lot of that is a function of constantly being in a crisis mode.

## 1b. If not, what are the impediments? Communication

[REDACTED]: We have had communication and collaboration meeting with CVM on biotechnology reviews. At a time there was impass because the technical requirements for the experts at CVM were very different from the CFSAN side of things. There were many meetings between the two Centers to resolve these issues. "Six Thinking Hats": we had all the scientists come together and think about how best to streamline the process. There are two different approaches and two different audiences. We have come to this point where it can work and both our opinions can be put in.

[REDACTED]: Not encouraged to talk to people outside the division; need to get supervisor's approval; there may be more within other divisions.

[REDACTED]: -Not knowing the focus, issues, and expertise of other groups; lack of interaction between Offices and Centers; and lack of time in schedules for dedication to effective collaborations.

[REDACTED]: -History of an organizational structure that says each problem belongs in its own little box. There were no larger mechanisms to do cross-cutting work effectively.

[REDACTED]: -The laboratory and the review teams need more communication. If we encounter a chemical with potential hazard, we could contact the lab to get more research done on that chemical. Right now, they don't know what each other is doing. You can always collaborate externally when you have a bigger issue.

-The biggest impediment is not knowing there are common issues. You need someone up top that knows what both Centers are doing and connect it.

[REDACTED]: Lack of discussion; tight management controls, even within the lab

[REDACTED]: -Issues are territoriality, misunderstanding of other Centers, policy issues.

[REDACTED]: Create more non-substantive opportunities for interaction

-If Offices/Centers disagree, it's difficult to resolve. In the past, consulted with CFSAN on a few issues: did not get a response from CFSAN and therefore did not make a decision.

-If the centers do not talk to each other, then we may not be able to identify an issue that affects both

-We wouldn't know what CFSAN is doing. It's a whole different group and so it's difficult. Need to work hard. Little communication, just incidental.

-The structure of the organization is all linear (stove pipe model), there is no cross, and it makes communication/collaboration difficult.

## Physical separation

It is a large Agency; staff are physically separated. There is even separation between labs that are next door to each other.

-Two buildings, lay-out of this building does not facilitate.

-Put everyone in the same room to discuss issues, maybe with a third party.

-Helps to be in the same room with people. If there is a geographic separation; people tend to go off their own and do stuff.

[REDACTED]: -[REDACTED] is over there and [REDACTED] is over here. Since I am over there I have no clue what is going on over here. When I was in the building there was a much more integrated approach to what we do.

## Time constraints

[REDACTED]:

- Collaboration is discouraged by the focus on bean counting/moving the freight
- Collaboration across offices and Center is as good as it can be (e.g., helping CVM establish their GRAS program); impediments are the individual time frames/priorities for each group.
- Mainly time constraints. Inter-office meetings/seminars are out there, but may not attend, or they start out strong but fizzle out. Attendance may depend on the issue.

[REDACTED]:

Difficult to find the time for collaboration. People are too busy.

[REDACTED]:

- The key problem is we have things we have to do and deadlines we have to meet. CFSAN has things they have to do and deadlines they have to meet. Helping us meet our deadline is not that important to them sometimes.
- Also, the timing issue - make sure everyone is invited, make the offer, alert them of the purpose of the meeting, and be up-front with them.

[REDACTED]:

Crisis mode is an impediment for coordination and collaboration. Normally you don't need a lot of coordination or collaboration if your usual stuff because you've worked that out over time. But it's when things come up, special issues and that's when the crisis mode hits. Don't think we do a good job coordinating in that. To improve it you have to devote some energy to it.

## Not valued

[REDACTED]:

Everything goes through the command chain: usually opportunities are identified by the management. Management lacks understanding of commitment to science; therefore, they tend to promote collaboration on non-scientific issues and discourage scientific collaboration.

[REDACTED]:

When you collaborate, more, it's more time consuming and not always valued. There are time constraints; therefore collaboration is discouraged to meet deadlines. Collaboration is driven by workload. Many good ideas and no time to see them materialize. Not enough resources.

-Tried to teach a course at [REDACTED] but was not allowed to go by my Office. Feels that he has the expertise but the Office said no. They are preventing his scientific work and it annoyed him. They should have asked about his workload. This should have been his decision. He wanted to contribute.

[REDACTED]:

-Just having the time to reach out. Also when having a meeting can you get all these people together at the same time? TSSRC does a great job because they announce well in advance.

[REDACTED]:

-There are no incentives for collaboration, thus they are rare.

## Nature of work

[REDACTED]:

Can't get data that other centers have (e.g., CDER). Example, components of food packaging: CDER has raw data files, but CFSAN can't get access due to proprietary issues. Can access summaries but not the data. If it's the same ingredient should have access to the same data.

-Proprietary nature is an impediment.

-We seem to not have access to data that's not submitted directly to us.

-It's rare that interest and concern coincide temporally. Even if a Center may have looked at a given issue, it is difficult to get them to look at something new and shift resources.

[REDACTED] ( [REDACTED] ):

- All collaboration is issue-based (e.g., collaborate with CVM on specific questions)
- Lack of follow-through from the offices can discourage collaboration between the lab and the offices. For example, a project may be initiated with a number of meetings, planning started, everyone seems ready to go. Then someone decides that the project is not a priority, and support is pulled.
- Because the different Offices have different product categories even though the science matters may be cross cutting there just sometimes is no time realize this other person is dealing with the same issue. There is a communication gap between Offices.

[REDACTED]:

- One of the impediments is certainly organizational philosophy. Two different philosophies tackling the same problem.

### **Not mandated/supported**

[REDACTED]:

- Not enough encouragement from office leadership.

[REDACTED]:

- Micro-management discourages collaboration; reduces morale. Upper management won't address these types of issues, and sends them back to the supervisors. Even though the organization set-up appears to encourage collaboration, within a given division, this may not occur.
- Often communication/collaboration is restricted by who the supervisors are. Often it is just a bureaucracy of personal issues the supervisors may have.

[REDACTED]:

- The problem is there is no accountability to be first a customer service person. If everyone would take their job as we are to serve those who call upon us and that is our job. There would not be all these trespassing issues. It's an issue of how you are held accountable.

[REDACTED]:

- Yes, collaboration exists across offices and centers on chemical safety issues. Coordination is not well established and is more informal. Sometimes they need to just go and ask. Would be nice to have a process in place to make research offices communicate.
- There is some collaboration between CFSAN labs and NCTR, with each doing a separate part to resolve an issue
- There is no formal coordination with research. There is communication but no formal process.

### **Other**

- Alternatively, on one occasion, they looked to another office for help who felt they were encroaching and put up blocks to collaboration.
- There may be some shyness about bringing to light that one office is struggling with an issue for fear that it might be embarrassing
- Disagreements have to be resolved by the management chains since they mostly occur between two "equal" parties.
- Other seminars, workshops, and symposiums would be effective but would involve money. People would like to participate but there are budget constraints.
- With the NTP nano-silver project - asked for a couple of things to be done but they were not done. They were on their own doing their own thing.
- Territorial, possessive , everyone has own agenda.
- The impediments are personal.

### 1c. What can be done to improve coordination and collaboration?

#### Exchange staff

-Establish relationships, despite physical separation. Establish interchange of people, formal detail process. It is good for people to understand what the other offices are doing, so when you have questions, you don't have to be afraid to ask for help.

-Some groups in one office could be moved to other offices (e.g., Dietary Supplements to Food Additive Safety) may improve coordination.

\_\_\_\_\_:

-Opportunities for the laboratory scientists to do details at regulatory offices and vice versa would be useful.

\_\_\_\_\_:

-Part of that comes back to short rotations or more opportunities to do details would help that. Rotation between Divisions and Centers should be mandatory - at least for new hires, would improve this, in part by adding more personal relationships.

\_\_\_\_\_:

Try to cross-train people or offer details in different offices/centers. This would also give you contacts for the future. Details are not very common within the Center and inter-Center, even less so.

-Could do more seminars, open staff college courses to other Centers.

\_\_\_\_\_:

In order to get a GS15 master rating, you should be asked to do a detail in some other unit so you could have a better sense of what we're doing.

#### Communication

\_\_\_\_\_:

Some technology to track what is being reviewed where.

-Improve internal transparency.

- Could use more information exchange. Can come up within one office, between divisions. Maybe regular (quarterly) meetings so people could plan ahead/have time to prepare something.

- People have shared research interests with the scientific community--it would be good to bring them together more. We have some focus groups that deal more with workplace satisfaction, but no work groups for shared interests and objectives.

-We need to figure out a way so people within scientific disciplines have a way to find each other. So when there are cross cutting issues that relevant for a scientist within a certain discipline they have a group of peers within that discipline to rely on.

-Monthly or Bi-annual Meetings to force people together and come to the table with issues.

-There should be an improved facilitation of interaction within the Centers and across the Centers. Comes down to training resources and increased communication across the Centers of different opportunities to cross interact, events that are going (i.e., talks, workshops). Just knowing who is doing what at the FDA. It's very difficult to figure it out unless people are publishing and very few scientists publish. So meeting people within the FDA is very difficult. You need one big coffee room.

\_\_\_\_\_:

-Get people together. Meeting the folks that you are going to working with face-to-face helps. Taking the short cut of teleconferencing. It takes a while to establish that. It should be balanced. Make an effort to attend meetings in person.

\_\_\_\_\_:

-It could be beneficial to have an internal/external database or just an update when we are working on a new chemical safety review, here is a brief email or a list somewhere about what is being worked on. It would be more efficient and also we would be responding in the same way.

\_\_\_\_\_:

-Lack of communication/interaction has always been the biggest problem. Every interaction doesn't have to be formal to be successful (e.g., \_\_\_\_\_ poster session for \_\_\_\_\_). Food conferences are good.

-On a more local level, host a complex science day between \_\_\_\_\_ and \_\_\_\_\_, poster session. This way the program personnel will have a better idea of the expertise and options available from the labs.

-Better communication and follow-through.

-Formal process for program and research offices to be engaged and improve communication. Research resources may be available that are not fully used due to lack of coordination.

- Have a point person at the Center level director. E.g., Everything is channeled through [REDACTED].
- Make one system like CARTS for CFSAN, CVM, and NCTR so we can look at the projects for all three. If I need some collaboration to complete my study then could look in the system to see who at CVM is doing something similar.
- It's in the middle manager's hands. They are the ones that should make the decision and give better direction down to scientist level.

[REDACTED]:

More roles like a CSO who manages a petition to the end through different disciplines--maybe someone who performs this function for the Center.

-Could/can assign a communications officer to certain issues: they coordinate, invite people, schedule meetings, and summarize outstanding issues.

[REDACTED]:

[REDACTED] has a [REDACTED] All-Hands meeting. This is a great asset to the Center. If we had that sort of meeting for each office, it could help. There may be more communication at higher levels, but the reviewers are not necessarily included.

-Two different groups with different overall goals may have trouble coming up with something that will work for both. Education of the groups so that each understands what the other does. Understanding is key to having people work well together (used Poster presentation at [REDACTED] as an example, and their visits to CFSAN in reviewing the GRAS program for development at [REDACTED]). If they know this, they can participate in making things work or can understand why it may not work.

Think we need to develop a better mutual respect and understanding of what each other is doing, what the expertise is. Management has to make a decision on whether they care about individual toxicologist and exposure experts reaching across the Center to assist or help the other Center. If it is not a priority of the management then it will not get done. We need a change in mind set; we all have to think differently that we are not really separate.

-So if the two Centers know what each other do on a regular basis there would be more collaboration. If they knew each other's programs and what was done day-to-day. It's not just when we have a special need that we start seeking each other out.

## Inter-grp mtgs/talks

[REDACTED]:

-Needs to be triggered by something; should be more proactive/informal. This helps to establish contacts  
-Bring everyone working on an issue together. Institute small-group meetings: Chemist or BPA "tea", brown bags, meet-and-greets.

[REDACTED]:

-Supporting forums for discussion, such as retreats. The Association of Government Toxicologists and the local chapter of the Society of Toxicology might encourage more informal discussion, hopefully with some means to spin off informal discussions into higher level meetings and/or National Academies' review panels to help address issues. Academia and industry could weigh in.

-We work in silos. Not much encouragement for information exchange because it detracts from the review process. A meeting is difficult to put together. The ICCVAM is an example of an established inter-agency committee whose job is to review and validate new toxicological testing methods. Objective is to come to a decision concerning the validity of a method. A pre-condition is comparison to the present gold standard or unique improvement. We need an analogous examination of trends and discussion of what's important to various agencies and why. Identify where we should do more coordination and not replicate each other's efforts.

[REDACTED] ( [REDACTED] ):

-Inter-office meetings to address red-flag issues; increased communication; inter-group presentations presenting the problem and ideas, and encourage others to make suggestions.

[REDACTED]:

-We need to improve communication. Help get others more aware of what we're doing and finding out from others what they need our research to do to answer their questions. Wouldn't say we need more meetings, but we need more meetings with a positive outcome, meetings where something is accomplished rather than just talking about it.

-Allow some freedom and allow people to state their case. To improve, have group participation. I have never been asked what needs to be done or what are critical issues. We are never allowed to speak with the leaders. We are left

out of those meetings.

■■■■■:  
Working groups.

■■■■■:  
Soft groups that aren't dealing with real policy issues and build discipline-based communities. Then start working on projects. So first would be an epidemiology interest group, a toxicology interest group, a compliance interest groups, where you start talking and building relationships.

■■■■■:  
-We could improve with informal meetings between people that do similar work. Foster some interaction.

■■■■■:  
If you want to do a good job you have to make sure that your reviewers aren't reviewing 85% of their time. The reviewers need time to interact with each other. Because CFSAN is one place, ■■■■■ in another place and policy people in a third place. How in hell are we supposed to interact with each other? Middle management (Branch Chiefs or Division Directors) should be made responsible for encouraging cross fertilization.

## Support from top

■■■■■:  
-Put in writing what is allowed/encouraged in terms of collaboration. Perhaps with a statement "Don't need supervisory consent to apply"  
-There needs to be some sort of cross-cutting management system to encourage/force harmonization across offices, first and foremost. And if this can be done between Centers, more to the good. This would seem particularly desirable between CFSAN and ■■■■■.

■■■■■:  
-It's going to require a clear commitment and active involvement of the highest level of senior management to tell the next level managers so that the office and division people know they need to do this.

■■■■■:  
-Trickle-down process: needs to start at the top and be supported across offices. In the past it was informal, but it takes time to build trust. If it is supported, there will be more trust

■■■■■:  
-Distributing the control or power of a group evenly across the Office. Not have one Office with more power over other Offices contribution to something.

■■■■■:  
Office of Foods need to play a role in this.

## Other

■■■■■:  
-Need to be able to go around management for this process. Provide direct collaboration opportunities between NCTR and toxicology reviewers for topics that arise. Each reviewer would have only a limited opportunity every few years to do this, so as not to take away from the review process. It could be dependent on the outcome of the research project.

-There needs to be some work on data sharing between the different Centers, ironing out the confidentiality issues, and processes for sharing that data from one Center to another.

-Data sharing in general

■■■■■:  
-For easing restrictions on publications: Perhaps instead of all publications going through your supervisor/division, a "courtesy review team" could be established that would assuage whatever the concerns there might be with allowing the article to move along in a timely manner. In other words, be able to get clearance either through the usual chain or via an alternate route without prejudice or retribution.

For access to CBI: We can keep info confidential and maybe an Executive Order or Congressional Action is needed to allow confidential business information to be shared across regulatory agencies.

-Need to make the system more interactive. Sometimes you receive "expert advice" that is not necessarily correct, but you have to take that advice. There should be an opportunity for two-way discussion on the issue.

-Keep other groups in mind when working on a project. Need to understand differences in approach and that it may be good to have some disagreement.

-There was a program (STEP, but was not sure what it stands for) where people from CFSAN/■■■■■ were sent to

NCTR for laboratory training (e.g., Learn laboratory techniques specialized in one area that is not his expertise.

- We need to gain an understanding of what goes on, what expertise is held throughout the Center and even within [REDACTED]? Here needs to be a way of getting that information out and allowing us to utilize the personnel that have these skills that we may need. Right now it's a laborious process.

[REDACTED]:

-It's a resource issue - identify priorities, have people that can dedicate the time providing the collaboration and doing collaborative projects. The CFSAN Strategic Research prioritization project is a good project to facilitate this coordination within CFSAN. However, the dedication of time by experts is a limiting factor.

[REDACTED]:

-Accountability. You have to be held accountable for a job badly done when it comes to collaborate with others. You can't tell somebody to do something when they don't know how to do it. We need to give them a set of instructions of what is expected and that is what you are measured against. Should be given feedback. This should be the job of the people that hold the scientific position, not the managers.

[REDACTED]:

-Index of expertise can vet with publications, etc.

-Once management has bought into the project, they need to get out of the lab. Let the PIs do their work, allow them to collaborate in the office and the field, and to determine in what direction to take their research. Don't tell the bench scientists how to do their research. Trust them to be well educated and knowledgeable in their areas.

[REDACTED]:

Try to create incentives although except for the lab/regulatory idea in 5c above the big problem is that other than [REDACTED] the chemical safety efforts in the other offices ([REDACTED], [REDACTED], [REDACTED]) are so small that it will be hard for them to reach out except in a limited way.

[REDACTED]:

If they are doing something a specific way, they should open up and consider different options. We can look at weight of evidence, critical studies.

-Safety factors could be debated.

-A risk assessment-based approach that factors in not just safety assessment, but exposure and other considerations would limit bias towards the type of study you give value to.

-More collaboration would improve.

[REDACTED]:

Be sure to be consistent even within a Center. Run into problems with different groups trying to do the same thing, but getting different answers because they think they can do better. If they don't like what we say, they may not include our information. This is difficult to resolve.

-We need to think broadly and be aware of who else [paper, guidance document] this will impact so as not to mislead.

## 2a. Are there sufficient opportunities for collaboration internally and externally?

[REDACTED]:

- There are if you make them; no formal procedures.
- Good collaboration with the lab (e.g., assistant office director detail). Lab tends to come over once or twice a month.
- Within the review team (toxicologist, CSO, environmental scientist, and chemist), we can get together anytime, and often do.
- Internally yes. Just need to use them. The weekly meetings help. Externally, this is difficult. Relationship with industry can't get too close because of our regulatory role, but can encourage them to work with FDA.
- Yes, but it depends on how well they work together. [REDACTED] has good collaborations with EPA (antimicrobials), USDA (meats), CVM (salmon)
- If it is a big enough project somebody will make the time for it and allow you to work on it. The biggest impediment is that nobody has time to call and coordinate

[REDACTED]:

There are some, such as internal details at other centers/offices. But if you go on detail, your work needs to be covered.

-External, interesting collaboration with WHO. Can apply to go, and it's a shorter detail without long-term commitment. Thinks this is the first opportunity like this in 20 years.

-No to both

Supervisor encourages people to collaborate: seek guidance from an appropriate expert, regardless of where they are (office, division, external). Supervisor can suggest someone for them to talk to; has a list of experts for issues/chemicals.

- Yes for both, when the situation arises. When they look into a particular substance of concern, the technical team does research; based on this, we can identify the expert in that particular area and can reach out.

-Yes. They are able to contract out certain animal reviews and can incorporate those results into an assessment.

Other offices may come to them for issues (e.g., Office of Nutrition for infant issues). There is good back and forth.

- Sufficient opportunities for those with well-established reputations.

[REDACTED]:

-Yes, there are opportunities, but a bad experience may make you reluctant to pursue them.

-In addition, there seems to be a lack of knowledge within the lab concerning what is available at other facilities for research, and a lack of knowledge within the offices as to the availability of the research group to do work for them.

-Program offices don't communicate with research as to what they need.

- No opportunities are presented by FDA as an entity; need to make your own.

-Unfortunately, not aware if they are asking for the data. Over the years there have been many cases where the Center "took it on the chin" for making what was perceived as a bad decision because they didn't have enough data. It was data we certainly could have provided to make a better decision.

-Yes, internally because of proximity of CFSAN and [REDACTED]. Externally the rules and regulations are prohibitive. Not easy to collaborate outside the Agency. Approval process.

- There are plenty of opportunities, but it depends on the middle managers. If they like that person or project they will say go ahead a do it.

-No, there is preferential treatment. How it got the designation of priority is based on those same group of people getting together and sorting out what is number 1, 2, and 3. Period. No open commentary periods.

[REDACTED]:

No.

-Motivated employees will invent ways to collaborate if there are resources and structures in place to facilitate them getting to know one another. [REDACTED] seems to be good at allowing people to do developmental details across divisions within the office. It would be cheap and easy to replicate that on an inter-office or inter-center basis. It is harder to do this outside of FDA but it would reap benefits if it could be arranged. A cheap and effective incentive would be to write such collaborations into IDPs and PMAPs: getting a top PMAP score and the resulting performance bonus would be contingent on a successful collaboration.

[REDACTED]:

-Works well if you are in a working group on a big issue that gets attention.

-Believes it would be supported if someone had an idea to do it.

[REDACTED]:

-Insufficient time for collegial interactions that would encourage familiarity with processes and expertise outside of a particular problem. -More formal/informal exchange programs would be nice, but there are time constraints. Cannot mandate this without stressing the system. Besides time the other impediment is not knowing who's out there in terms of expertise.

-Internally, there are e-mails for proposals/projects you can work on. Work with OR.

-For research, there is good collaboration between the Centers and NCTR. For the review process, collaboration with within the center (internal) is pretty good. External collaboration requires clearance.

-Nothing is holding us back, no impediments. Need to reach out to form a relationship, like we did with the GRAS compounds to learn more.

- [REDACTED] is supportive of collaboration both internal and external. On a case-by-case basis some groups have more internal collaboration than others.

-Within [REDACTED], there are sufficient opportunities because we are a small Center. We know each other well and they organize social events.

-We never had any impediments to collaborate. We go to regular meeting for AFCO. In fact AFCO has one of the large committees of lab services, the methods committee, where we look at method needs to be updated here and there. We have 3 meetings per year, 1 with the AOAC and 2 separate meetings. There are sufficient opportunities for my group to speak to our compatriots in the States, at universities, and also within industry.

## 2b. And if not what are the gaps?

### Communication

████████: -Different offices work on the same type of project in different areas/aspects, and they may or may not get together on that.

-Maybe we just don't know what everyone is doing in the different Centers with respect to research. What are they working on in █████ exactly? What are the different groups working on and what are their capabilities? It probably cuts across to NCTR as well.

████████:

-The laboratory and the review teams need more communication. Right now, they don't know what each other is doing.

-We need better coordination between labs and the regulators.

- We need better coordination between labs and the regulators. The pathways not there for routine talking back and forth, communicating issues. Need to set those up.

-Lack of communication within the Center is a big issue and has been that way since I have been with the Agency. E.g., we get a printout (about once a week) which essentially details the different efforts that are ongoing of a regulatory nature across the Center. Have talked with other people in the Center in other Offices and they are not even aware of that. There is this lack of knowledge. We just don't know our neighbors. Our offices are separated and we might as well be in another country. Now we are just across the parking lot and we still don't know what is going on. Often there are studies being planned that we actually could contribute to but people planning the studies are not aware of our expertise.

████████:

-Program offices don't communicate with research as to what they need.

████████:

Lack of communication with others about similar products (CFSAN, EPA)

### O/S Mission

████████:

-External collaboration is not perceived favorably because it is outside the scope of CFSAN's mission and resources are a problem (cannot be transferred). Sometimes easier with other than agencies because industry cannot fund work. Limited collaboration with external sources on safety reviews, but it is limited; case-by-case basis.

### Hierarchy

████████:

Ad hoc is more difficult. Need to identify the expert, convince your supervisor

-Maybe we just don't know what everyone is doing in the different Centers with respect to research. What are they working on in █████ exactly? What are the different groups working on and what are their capabilities? It probably cuts across to NCTR as well. If you want to improve this, we need to understand the specific knowledge skills and abilities that each of the people and the facilities have.

-Usually CSOs and supervisors for interagency contacts, it's rarely reviewers.

████████:

Based on details, there is a difference in cultures between the buildings. In this building, they are encouraged to explore new disciplines and have opportunities for training in different areas; in the other building, they are discouraged from specialized training because they are not an "expert" in the field. If the supervisor does allow it, but upper management is not convinced, opportunity may be shut down.

-The management structure tends to be vertical and hierarchical both for offices in CFSAN and between centers. This is inevitable due to human nature in the absence of any proactive upper management attempt to foster a cooperative, interdisciplinary climate.

--The hierarchical nature of the organization means you have to go to your supervisor to ask for the time, through the division head, and then maybe you can talk to someone. Don't control your own time for this sort of thing.

Externally, there is a culture of secrecy. The Agency does not want to say anything or work with anybody from the outside that may interfere with our making enforcement decisions or regulatory actions. We don't have a grant/funding mechanism that is very robust for getting research done with the outside.

[REDACTED]:  
-We do have multiple groups working on chemical safety of particular chemicals. However, each group is an entity unto itself and only the people working in that group and the managers know what is being discussed and what the conclusions are. Any information that is available is not made available to those outside the group. There is no information sharing. We don't know what the conclusions are. The managers are aware of the information from all the groups, but that stays with the managers. The policy is a need to know basis.

[REDACTED]:  
I often feel that there is an underlying sense that I have to justify my collaboration with other Centers. For example you're working for CDER or [REDACTED], don't you have anything else to do? When I joined the Agency I thought collaboration was my number one measurement stick. How well can you build collaboration with other Centers? It was weighed high on my PMAP. Also it was weighed higher for an interagency collaboration than a collaboration with the scientist next door. There was a hierarchy in that. Now I think it is the opposite. If you want to collaborate with another Center, you have to make sure you take care of everybody in your own Office first. You also have to defend it or justify it now.

[REDACTED]:  
-Collaboration generally occurs only through personal "networking". Although there is "lip service" about regulatory staff working with laboratory scientists, there is no management interest in, much less requirement for attendance of the respective staff at each other's meetings. So it won't happen unless there is a mandate from higher up that is some point in the career of the staff scientist (lab side or regulatory side) that this is something they should be doing and they'll get a rating on.

[REDACTED]:  
-Road blocks: prohibitive rules and regulations. At the bench-level must work with scientists locally. Relax restrictions so that more people would participate.

-They need a very strong scientist. We need to look at CV's of each principal investigator in the foods area and know where expertise is and know what our expertise is and know what the gaps are. Until you know what your team looks like, how do you coordinate a team? This person should be senior and have knowledge in both clinical and animal research, not just a microbiologist or toxicologist.

[REDACTED]:  
Lack of time, red-tape processes that slow things down.

-When I see it happening it's scientist to scientist, that have established relationships, and it's not management to management who supported that relationship.

[REDACTED]:  
Any opportunities that exist are created by the staff when the need arises. There is not a lot of crosstalk because there is no current means. The pathways not there for routine talking back and forth, communicating issues. Need to set those up.

## Funding

Not enough opportunities (people, time, money) to go to industry meetings. Can meet on an individual basis for a question or by issue. Try to encourage pre-notification meetings to discuss issues of concern.

-Travel/budget constraints. You used to be able to attend one conference/year, no questions, but now it's more difficult. They are really cutting down to what is directly relevant to the job. You can't collaborate if you can't go.

-Lack of time and cross fertilization and cross communication.

## Coverage

If you go on detail, your work needs to be covered.

-Time constraints. Everyone is too focused on their own responsibilities/areas of expertise. Difficult to keep up with what other groups are doing. Not enough opportunities for people to get together and share.

-The obstacle here is that supervisors will lose effort towards regulatory review assignments, so they need to be given incentives (people, performance bonuses) too. There needs to be buy-in throughout the supervisory chain that

diverting resources now committed to regulator review into these collaborations is supported.

-People don't have time for collaboration. An individual may have an idea but the person that could help (other party) does not have the time for collaboration. Or it could be the person's boss, he or she does not have the time to take care of it. Also, people would wonder why you have all this time to do extra things. We are very busy with our mandates, industry fees. So you have to balance anything you do outside with your review work. If you put your effort in the wrong place your other things will suffer and you won't meet your performance goal.

██████████

If you want to collaborate with another Center, you have to make sure you take care of everybody in your own Office first. You also have to defend it or justify it now.

## COI (industry)

### ID of partners

People don't know how to go about it.

Works if you know someone.

-Difficulty in maintaining a directory of scientific expertise. Has been tried many times. "Traction" in-house social media program that may be a pretty good way to do this.

- We don't know anyone, so can't figure out where to start.

-Looking for opportunities and trying to figure out who to collaborate with. Trying to identify resources. There has been talk about some kind of Subject Expert List, but apparently that is not supported by the higher ups.

-I would like managers to be supportive of collaboration. I would like enough information is spread around to the groups. That if I wanted to know something I would have a pretty good idea where to start. That's a frustration.

You have an idea or question but you have no idea where to go to ask that question.

-Don't know the people at CFSAN that well. Knowing what other people do.

### Other

██████████

-Collaboration is neither discouraged nor particularly supported. Basic research is discouraged, especially with industry-sponsored substances. Recently involved in collaboration with NCTR, NTP, and █████ on a contaminant (melamine), but this was different because it was not a sponsored substance.

- Not easy to participate in. There are details and shadowing, but it is difficult to have less formal/cumbersome opportunities.

-Not enough done to bring along skilled but less experienced people and involve them.

Mentor/develop less experienced people would benefit program; turf issues may discourage this. A succession planning program would help.

██████████

-The gaps are being able to participate in those opportunities. There is insufficient time to be able to participate in collaboration.

██████████

-Lately, I have been working with label data and merging market sales data. We heard that another Agency was working on the same thing at the same time. If we could be purchasing and using these databases together it would save a lot of time and expertise or we could be doing it at a more efficient pace.

## 2c. What collaborations would improve/benefit the programs?

-Different offices work on the same type of project in different areas/aspects, and they may or may not get together on that. For nanotech they are trying to bring people together.

\_\_\_\_\_:

Could use more contracts; helps supplement what is done in-house. Need the contracting process to be more efficient and stream-lined, and keep in the loop. This is an administrative issue. Not kept in the loop and not always sure who to ask.

-If we get some chemicals in that we don't know a lot about we could send them to labs (\_\_\_\_\_ and NCTR) and say we need this type of study done on it.

-Detail opportunities would definitely help, but people are strapped for resources.

\_\_\_\_\_:

-More collaboration is needed with academia--there are not the issues here that there would be with industry.

-Allow talks on areas of specialization within the Agency, rather than restricting presentations to general topics or boosting someone more junior because a more senior person wants to go and should represent FDA.

-Less red tape for when you want to go somewhere.

-Talks could be vetted before you go to address any issues that should be protected.

-Within the division there should be more collaboration between chemists and toxicologists

-Early notice of when the researchers have papers accepted for publication.

-Endorsement of a cooperative, interdisciplinary climate by upper management would improve efficiency, reliability and credibility in the present era of markedly increasingly complex biomedical science and safety assessment.

-The most valuable improvement would be a manifested interest on the part of management and the review structure to look for things that might be of common interest.

-\_\_\_\_\_, staff college: but some topics are not relevant; could streamline to be more useful. Workshops/training could be more tailored to certain divisions/centers (e.g., botanicals need more opportunities). They do offer some courses within the division, but Agency-wide would be more helpful.

-Could benefit from collaborations between Food Additives and New Dietary Ingredients (there's no reason these have to be different departments). More collaboration with infant formula, food safety people, UMD/\_\_\_\_\_

-Topic-based collaborations.

-More collaboration with local universities. It would help and they are desperate for the money. Because they are so desperate for money they're more willing to listen.

-Not a specific collaboration, but eliminate bureaucracy that is involved with getting support. Within some groups it not a problem, but with other groups you have to follow the chain of command all the way up and all the way down.

\_\_\_\_\_, \_\_\_\_\_:

-Could have internal risk-assessment-qualified people check the data before we put it out externally.

\_\_\_\_\_:

-Stronger collaboration with EPA's ORD and analyzing new and emerging science. A stronger collaboration with International Life Science Institute (ILSI). Decrease collaborations or input with National Toxicology Program (NTP).

\_\_\_\_\_:

-Quarterly meetings that are mandated: people encouraged to participate.

-Could have a smaller group coordinating, developing goals, and prioritizing topics. The agenda could be planned a year or 2 years in advance. People could plan on the meeting.

-A good model would be IRAC (Inter-Agency Risk Assessment Consortium), although this is a more formalized situation.

\_\_\_\_\_:

-Need more active interactions with academics and other regulatory science agencies.

\_\_\_\_\_:

-Use the \_\_\_\_\_ model: can interact with faculty, students.

-More collaboration would be helpful. Bring up to speed with state of the art, but off scope and mission. Need more flexibility, and innovation to improve whole center. In some cases, research that appears to be off-mission may have a long-term benefit that is not immediately obvious. Bring in academics/institutions to help bring innovation.

\_\_\_\_\_:

We should take advantage of collaborations with EFSA and others.

-We don't always exercise these options. If we have an agreement with them, we could consult with them on decisions. Should try to work on some international harmonization for issues like allergens.

-Need to be at some of these international meetings, but with budget cuts, everything has to be "mission critical".

-For certain chemicals/ingredients, we need to be part of the conversation to share expertise, stay cutting edge.  
[REDACTED]:

-NCTR research. There are some crosscutting issues for nanotechnology. Some staff members have been sent to NCTR for nanotechnology training.  
[REDACTED]:

-Offer opportunity to write mini-grants to pursue work with others; this could also highlight research that is ongoing in the center.

- Difficult to stay abreast just by reading an article. Could try using academic experts, like in Europe, but it is difficult here, because the academic review is in a different format, and would still have to do an assessment in-house.

-More communication with others about similar products (CFSAN, EPA), even to know whether they have looked at a given product or have done something for it.  
[REDACTED]:

Something like IRAC. Don't think there is anything like that for the toxicology community or the chemical safety review community. Perhaps there should be some sort of interagency or just across the Office of Foods or FDA. Toxicology groups that get together and talk about issues and try to come up with some position papers or something like that on common issues. Some sort of forum.

### 3. What toxicology research could NCTR do for CFSAN or CVM that it is not doing for either CFSAN or CVM?

(b) (5)

[REDACTED]:  
-Resolution of pre- and post-market safety issues; refinement of current testing systems so that more relevant human toxicity can be covered by animal testing; continue to explore whether emerging technology can help chemical safety review as a supplement to existing methods. Redbook allows use of alternate methods if you can justify them; NCTR could help in the justification process.

E.g., NCTR backed FDA's decision on BPA. It would have been a problem if their results did not corroborate  
-NCTR does a little bit of chemistry research (b) (5)

[REDACTED] They tend to operate independently. A closer relationship would help improve working relationship. Not sure of all that they do and probably v/v.

[REDACTED]:

-NCTR does a good job of making research relevant to regulatory needs. Addressed well, but emphasis on botanicals (complex mixtures and must be considered directly). Should examine how much we invest/explore in this area. Take on bigger research projects but sometimes you need a small study for a small question. Literature searches are conducted but not shared.

-Could be evaluating and validating new methods being developed for toxicity testing, especially as part of this Tox21 effort. There are lots of labs that are developing these new methods that fall under this umbrella of TOX 21. FDA regulators could benefit if FDA researchers started to weigh in on which of these methods are the most useful and for what.

-They could work on the development of immune detection methods.

-Research on fluoros, especially the new C6 for fluorinated compounds, the perfluoropolymer alcohols in particular. Validating alternative assays. OECD does that too. NCTR could help us when we come up against problems, like the (b) (5) problem or more data for particular compound that is not available and that we need really quickly.

-We are corresponding more regularly. They are now asking how we can support you. Our [REDACTED] group came over to the Office and asked what can we do for you? What kind of research do you need? (b) (6) of NCTR always asks, "What can we do for you? We are here to support you." The message has gotten across.

-Endocrine disruption testing

[REDACTED] ( [REDACTED] ):

-In vitro testing. Apply new technology: genomics, proteomics.

-They have meetings with NCTR: they can work on a substance, but not necessary to his work. It would be a duplication of effort if they do the same thing as the stakeholder.

- NCTR is already doing a lot of research that impinges particularly on CFSAN and [REDACTED]. They would like to do more research to support the regulatory centers (cosmetics, dietary supplements, botanicals), and are continually asking CFSAN and [REDACTED] for relevant projects to enhance our ability to assess safety. NCTR is still under-utilized; they are our "best collaborator."

-Other substances, maybe already regulated, that could be looked at again (substances are identified in the JECFA reviews under the recommendations for further work).

-Post-market questions

[REDACTED]:

-The process that could be enhanced by removing the NTP component and have work done directly for CFSAN and [REDACTED]

[REDACTED]:

-It is the responsibility of the Centers to communicate with NCTR of what type of research they need. It is driven by funding.

[REDACTED]:

-The allergen team in CFSAN could use more toxicology research in terms of allergenicity.

[REDACTED]:

NCTR is currently, and has for many years done major toxicology studies for both Centers. What we need is for the local ([REDACTED]) labs to do more short-term studies related to current regulatory data gaps, which are probably too small in scope for NCTR.

[REDACTED]:

The best thing they do now is large 2-year studies; multi-species studies. Should continue to do.

- These studies should be done as a last resort if a pilot study conducted at [REDACTED] does not yield results.
- Alternatively, we can save time by confirming a study is not needed (e.g., [REDACTED] dosed at multiple levels in melamine study vs. the proposed protocols--saved money)
- There could be better coordination between NCTR and [REDACTED].
- Melamine - NCTR did some 28-day feeding studies. [REDACTED] replicated with oral exposure (feeding vs. gavage). With oral exposure, levels increased the toxicity 10x (4 days to tox). Labs here can do short-range dosing studies. They can do the longer studies.
- Not sure. There is a lack of communication between [REDACTED] and NCTR. It seems that NCTR's needs are met first.
- NCTR operates at a different level, they have their finger on the pulse of science: cancer induction, generational toxicology, genetic mutation micro-arrays. Management does not pursue this relationship. They should allow individual scientists to pursue their own collaborations with NCTR. It would be beneficial to join a core group at NCTR on a specific topic and collaborate with them on that kind of research.
- NCTR has a larger program and capacity, more resources, and can do a lot of things CFSAN cannot. CFSAN requests studies to be done by NCTR (from program offices and more detailed) on a case-by-case basis or chemical-by-chemical basis.
- Nanotech and mixture exposure of multiple components. Also, we must have our own capability at local centers and can't give everything to NCTR to do for us.
- Don't know, we are going to visit NCTR to talk to them and find out.

[REDACTED]:  
A significant fraction of the NTP/NCTR IAG is devoted to CFSAN (and to a lesser degree) [REDACTED] research. Examples include projects on "cooking carcinogens" like acrylamide and furan). It is unclear whether there is buy-in from OF/CFSAN leadership into these projects. There is more capacity for such research at NCTR and NTP but there needs to be more engagement from OF/CFSAN/[REDACTED] leadership which includes selection of projects that the leadership agrees is important. One area that NCTR AND MODI/II might expand into is method validation. This is tedious and not at all "sexy" but unless new methods are properly validated they are not going to be interpretable or acceptable for regulatory use. One idea would be to make FDA labs the center of ring trials and other validation efforts to give government imprimatur on these efforts.

- Trying to get them to study mycotoxins as classes of chemicals instead of one at a time. Study fungal contamination as problem of the fungus, which is a mixture of toxins, rather than looking at individual toxins.
- What they do is very good in identifying what needs to be done, but once they find the low dose threshold area, it would be nice if they went back in to find more dose response in that area.

[REDACTED]:  
-Possibly they could develop a human serum data bank for access to human data to supplement animal data.

[REDACTED]:  
-No ideas for other things: need ongoing conversation between [REDACTED], [REDACTED] and [REDACTED] so they don't duplicate efforts. Some overlap is OK. Programs need to be complementary.

- Would be good for training on methods/techniques.
- Doing much better: more focused on collaboration. She is collaborating with them on nanotech, but she was proactive in getting involved in this. This seems to be mutually beneficial. She can be a part of research in this way.

-Chemical-chemical research. We don't have enough data to address this. When we look at safety issues, most risk assessments are based on individual compounds, even though we are always exposed to a mixture of things.

-We need small studies done quickly. We have to start talking about what capacity you have to do those and still keep on target with your bigger research projects. Also to share local expertise, what does NCTR do? Four or five years ago NCTR went around visiting various Offices at [REDACTED] talking about their program.

-It would be something like acrylamide, which NCTR was involved with acrylamide in both animal feeds and human food. It would have to be something not subject to what we require in a submission approval for a FAP or GRAS item. Something extraordinary within animal feeding, like a new mycotoxin. NCTR could possibly do a rodent study.

[REDACTED]:  
-How could we possibly tell when most of us don't know what NCTR does? There are a few people that sit on NCTR panels and they know what is going on, but the information is not disseminated very well because who's got time.

## Interaction With Other Programs/Agencies/Public:

### 1a. Are those conducting chemical safety risk assessments and safety reviews obtaining the type and quality of toxicity and exposure data they need from laboratories in CFSAN, CVM, ORA, and NCTR?

[REDACTED]:

They can if they know what to ask for.

Yes.

-Yes. We don't always get everything we want, but it is type and quality.

-For pre-market, have to rely on the petitioner. -For post-market or a particular risk assessment, yes we do get the information we need. It can be slow to get the ball rolling, but industry, the labs, and contract labs have been very helpful.

[REDACTED]:

-In short-term yes: NCTR is performing needed studies.

-Occasionally the research scientists ask what kind of data/research is needed to support regulatory decisions, but usually division personnel cannot come up with an idea on short notice.

-When you have research that needs to be done, it may be complex. To get it done, you have to follow strategic guidelines (staff scientists are not encouraged to attend these meetings)--which limit the type of research that can be done

-Yes. But not sure there is sufficient expertise coming out of academia to support our current regulatory paradigms. Academia is moving to cutting edge (in vitro, etc.), but FDA uses what's validated (in vivo, animal model expertise). More prohibitions now against working with animals now. Will the new scientists understand the paradigm under which we're working?

-It appears that the exposure data do not accurately capture the facts, based on one particular compound for which the interviewee's intake level was much higher than that used in the calculation. Feels that there may be mindsets here that might prevent broader examination of available data and support for acquiring new data [REDACTED] (b) (5)

-As a regulatory agency, we should not be involved in research.

-We (FDA) cannot share all of the information and don't have access to other information: a lot of the toxicity information is not sharable. We share to the extent that we are able. Exposure data depends on market information that we don't have access to. Don't know to what extent certain food additives are being used; we have more information concerning certain foods

-To improve type and quality of data, would be helpful to make research conducted at [REDACTED] relevant to the center's mission. However, this may not happen because they don't have enough of the types of scientists they need to do the work.

[REDACTED] (b) (5):

No.

[REDACTED]:

-They are when the needs concern traditional regulatory toxicology issues. The problems arise when external sources expect to drive the regulatory assessment without understanding the regulatory process, the evaluation paradigm or applicability of certain research/information to a safety assessment

-We've collaborated with research chemists at CFSAN on exposures of particular chemicals and you may have to do a food survey and analyze for the chemicals in the food.

Also we have a project underway with the University of MD. Yes, we can go to research scientists for exposure data. We wouldn't ask them to do toxicity studies because it is the industries responsibility. We do have programs to look at exposure data for particular chemicals in the food. This is a very good program. We did collaborate with NCTR. (b) (5) - information used in risk assessment.

[REDACTED]:

For many years I have tried to suggest experiments to my friends in the labs, but without management support, these suggestions have gone nowhere. Recently I have been asked by management to make such proposals formally, but these again have gone nowhere because the labs expect money to come with the proposals. Labs may need more funding to do such studies, but no experiments suggested by regulatory staff will be done unless we have some

control over which studies are funded.

■■■■■:

- Would like to be in on discussions (even one representative) selecting compounds for NTP and NCTR to work on. Believes they could contribute to smaller, faster, still informative studies
- Going to start to due to more interaction. If you know the need is there, research can be more focused.
- If you don't have the expertise, a project officer can write a protocol, bring in ORISE fellow to do the work for 2 years. Limited project with target outcome. The combined office and research support would then get the funding
- Can build a team across offices to address this issue.
- There is interaction when possible. The lab interacts with NIEHS on issues like NTP (National Toxicology Program) and nanotechnology.
- I hope so. Several projects underway for cosmetics and nanotechnology. Offices need to request research and identify the type of study they need. If it can't be done here, they can be directed elsewhere.

■■■■■:

In terms of exposure data, yes.

NCTR work on BPA, melamine, acrylamide and furan has been or may be very useful. Testing of botanicals is more mixed. Example: by the time they tested usnic acid and published the results the industry had moved on and you couldn't find the product on the market. ■■■■■ pig capabilities should certainly be better exploited by CFSAN.

■■■■■:

Health Hazard Assessments: if there is a recall, then we coordinate with them to investigate for contamination. That process works well.

-It doesn't appear that we usually wait for data from them to help with assessments: probably don't have access and would not wait. Reviewers are used to dealing with uncertainty in completing their assessments.

■■■■■:

The laboratories in CFSAN and ■■■■■ provide a lot of relevant information. ■■■■■ analyzes sample for us all the time and provides. It is difficult to know whether they could do more because not sure of priorities, who is directing ■■■■■, what is the chain of command to make a request.

## 1b. Do FDA scientists have access to information from databases at NTP, NHANES and other agencies/sources?

[REDACTED]:  
-Other agencies can be tough. Worked with (b) (5) on a (b) (5) that was related to melamine; asked for info to help with exposure assessment, but they would not help out.  
-Sometimes (b) (5) won't share tox data.  
- NHANES provides good raw data, but need a contractor to process

[REDACTED]:  
Harmonization is laudable goal. But, each agency needs to harmonize within before we can think of essentially national, really international, harmonization. Can't even get local harmonization.  
- Mintel (New Product Database), [REDACTED]. FDA should develop its own food product label database. Believes industry would participate voluntarily, and FDA could enter the rest of the info.

[REDACTED] ( [REDACTED] ):  
EPA risk assessments.

[REDACTED]:  
EPA's IRIS is available online and other toxicology assessments that support the IRIS document are available online. National Academy of Science (NAS) documents online. International Agency for Research on Cancer (IARC), OECD - Screening Information Data Set (SIDS) are available online.

[REDACTED]:  
-I have worked hard personally at establishing a contact and a collaboration with that Agency. There is so much apprehension and paranoia of working with another Agency, still see that when it comes to (b) (5). Think it is toxic and unhealthy. There is nothing to be gained to have a baseline attitude to not to be working with other Agencies in your area of expertise. You must. That's the way you learn and how you get different perspectives. This is not highly supported.

[REDACTED]:  
Yes. Also IRIS, ToxBase, ToxNet

[REDACTED]:  
-Have access but it is limited, no access to raw data.

[REDACTED]:  
Outstanding access to NTP, NHANES, FDA library resources. Need to maintain that access. We have some of the top access internationally of any agency--we cannot lose this. Can get articles within 0-3 days.  
-Can use PubMed, Agricola, etc.  
-FDA Field Accomplishments and Compliance Tracking System (FACTS).

### 1c. What additional databases would be beneficial?

[REDACTED]:

Industry use database would be very beneficial.

- However, we can put too much stock in databases. Need to know how up-to-date they are.
- Just because they're there, does not necessarily mean they're useful. Old data may stay in when no longer relevant.
- Cannot replace information you would get directly from industry, which we're not able to get right now.
- An internal FDA database.
- Survey data from USDA (market basket/food consumption data)
- Recently added some useful ones, "Big Three" consumer survey groups: Mintel Food Essentials, Gladson, access to Nielsen (labeling group) survey data.
- With [REDACTED], could get exposures that are more than just food exposures; need to go to EPA for real exposure assessment.
- CDER/EPA databases
- Longer-time-frame consumption data; market share data on uses on food and packaging to complement what we have.
- Before CDER could be asked but problems with sharing data because of CBI issues. Same with EPA, a lot of their tox data are considered CBI. We've acquired some databases for food packaging - what's coming up, what types of packaging is being used, how much. Important databases for us to help evaluate food packaging materials. We need to know what is out there in the market place and what is changing. Having access to these databases is great but having continued access to these databases is better. Then we can monitor trends in packaging.
- Market Reports (but need to pay for) to get idea of allocation of processed foods. You can get some idea from USDA. Get an idea of the extent of market share for certain things. We have some label information, but thinks there are some larger reports. Example: Bag salad market would be of interest to food contact and us, Division of radiation.
- Databases that map out subpopulations (infants) or sensitive populations; high risk groups

[REDACTED]:

QSARs have a definite/positive role at the early stages; especially for relative toxicity in a given class. FEMA (Flavor Extracts Manufacturers Association) has done work with this. Make risk assessments based on QSAR and SAR, but this works because they are dealing with very low level exposure.

- Some have to go through the library; some are unavailable due to budget constraints. The BioSciences Resources Center or the library can find references, but there is a 3- to 4-day delay.
- IARC, EPA, ATSDR. They have raw data. We are able to see summary data, but it would be nice to access the raw data.
- Historical databases. European database RITA (Registry of Industrial Toxicology Animal data);  
<http://reni.item.fraunhofer.de/reni/public/rita>
- Getting information from other agencies is a different story. It all "depends." Some Centers are more than willing, but other Centers (b) (5) [REDACTED] forget about it unless you can get it informally, but officially forget it. Understand there are issues with confidentiality, but if we are asking for non-confidential information it should not be a problem.
- TOXNET, PUBMED, and those kinds of things without having to be restricted to just the abstracts, getting the full publication.
- Access to in-house databases CDER, CDRH (devices), and CVM

[REDACTED]:

The pathology safety review is often forced to look at what is called the historical control data which is the baseline data of the change that we are looking at within the animal strain that is under investigation. There are data sets in Europe that are industry driven, but independent in the assessment. Refer to handout for Registry of Industrial Toxicology Animal [RITA] data - continuous advancement of rodent tumor data acquisition and interpretation. Europe. The membership fee has prevented FDA to having access to these quality data. For the quality of science we are talking about that access would be necessary.

[REDACTED]:

If the NIEHS Tox21 and ToxCast program develop a database of information, eventually will be available.

[REDACTED]:

More Nielsen Market Sales Data (we have stopped purchasing that and it really helps with post-market analysis of additives). More label data (we need to rebuy or update what has been purchased in the past for tracking over time

to see if things have changed). Things that are not provided in our current databases. Everyone wants these post-market updates every 2 years. The database data is only updated when the research is there, every 10 years. The analytical data for post-market updates can show you these quick turnovers. So, more analytical data on the topical concerns of the time would be nice.

████████:

-QSAR databases; Quantitative Structure-Activity Relationship (QSAR) available at CDER; easier access would be nice.

-Does not know if we have access to information from Defense or Commerce. There should be databases available on the international level (Europe), but really don't know. Specific areas such as mixture toxicology. Nanotechnology too new and so no database available.

-Longitudinal extant data - survey data that already exists. What was happening in humans over time?

████████:

List of available, and of programs conducted within the Agency--a clearing-house.

-We need better long-term (chronic) food consumption survey data

-Not sure we can get access to actual raw data from NTP; sometimes in the future it would be useful to get the raw data so we can manipulate it as we want or need versus just the end result summary data. Access to the raw data from NCTR.

████████:

More would be nice. Can go to people within █████ to do analysis. There are not many good databases, and some are expensive. We are sitting on a lot of good data that we already have (e.g., recall data) that we could do more with (look at root causes, what caused the problems)

████████:

-Should look into this. Doesn't know if he might get access to NTP primary data as opposed to just a summary of results. It may be possible, but not sure.

-There are a lot of databases out there, rather than one standard database or sources of data. Not all are valuable. People use different databases--one may be successful, one may not--but they come to a meeting having looked at different information. The inter-library will also conduct a search of a collection of databases for you. It might be nice to have a statement identifying the search from which information was obtained.

-Do not have access to all CFSAN databases (e.g., ADI database) some would be useful for feed ingredients and GRAS reviews. We have access to internet, not intranet (or S-drive).

-It would be helpful to organize the ones we have so that we know what is available. This needs to be done at a higher level. Now it is up to individuals to find whatever they can find, and we may not know what all is available.

-Nothing within the Agency but what other countries are doing. The unique aspect of residue we look to see what's going on in different parts of the world.

-One suggestion. Could the computer people automatically link PubMed with the full journal articles? If we go to the library website they are linked automatically. But with PubMed there is a disconnect with certain papers.

-in silico - predictive toxicology, computer predictive database would be helpful. Also, there are people with particular expertise in toxicology that we just don't have and it would be nice to know if they exist in the Agency and where they might be. Traction - share ideas through resumes that would be a start.

-Access to as a residue chemist is information on international drug approvals and the risk assessment exposure mitigation parameters that different regulatory agencies have put into place. We have a collaborative arrangement with Health Canada, EMA (Europe), and personal contacts. It would be nice to see what the drug label for a product looks like in Australia. We can get to the Codex final decision website to see what they have done. JECFA is lead in to that. It would be really helpful if we had access to these other regulatory agencies' basis for approval.

-Databases within FDA - search for chemicals that are reviewed in other Centers, integrate preclinical and clinical studies, integrate and search

-Database of analytical methods that is easily accessible and rapidly performed.

████████:

-Protein database searches, DNA database searches, SIRN database searches, and the new molecular data

#### **1d. What do you see as barriers to us getting this information?**

████████:

No procedures in place for sharing, or if there are procedures, they don't work well.

- Possibly a mandate would help to get industry to share more information.
- Do not have many tools/computer programs to extract the necessary data.
- Money. Lack of knowledge as to what's out there.
- People like to hold on to their own stuff; wary of sharing, even within the center. Lack of awareness about what is available.
- There are financial barriers to purchase, maintain, and renew. There are some proprietary issues.
- Money; go-to person to identify data sources and follow through
- Monetary. Also validity issues, have these databases been QA/QC'd, they have to be publicly available.  
[REDACTED]:  
-Confidentiality. It would be helpful to have an agreement between the Agencies and industry to collaborate to get a product through.
- The barrier for EPA data is time: usually these data are publically available, but we can't get it in a timeframe that is useful. CDER data have legal barriers; we can't get that data because the sponsor owns that data. Even though we are the same agency we don't have access to that information.
- Information may be proprietary or trade secret so it cannot be obtained. Suggestion would be to have limited access to databases from other Centers within FDA.
- Funding. Sometimes the data are in raw state and need to be manipulated to get into a useable format. Trade Association may want to give us a database which may contains production values or recipes for food products. How and can we keep these data confidential under the laws?
- For internal information it's paranoia, a knee-jerk response to confidentiality. When I do need information I call some lower level people. If you go the official route it may take a lifetime.
- For databases: cost  
[REDACTED] ( [REDACTED] ):  
Communication: address issues properly and with the right person; difficult from the staff level to get to the right person.  
[REDACTED]:  
-Usually the commercial data sources are complicated to go through the process (purchasing access). The ones that come from public health agencies or other organizations (theoretically available to the public) are not well designed so takes time and effort to be able to use it.  
[REDACTED]:  
-There has been a communication problem for years, but is getting better due to strategic planning.  
-No barriers for accessing databases to obtain summary information; but not possible to get detailed study data.  
-Not seeking it. There is no continuity when there is a change in administration.  
[REDACTED]:  
-The NTP informatics group is very good at pulling data for us, but not sure everyone at FDA knows of their willingness to help.  
[REDACTED]:  
For the labs, we don't always know what the research capabilities/expertise are. Need a good way to look for that. Difficult enough to figure out what OR offers and keep people aware of that.  
For NHANES, access is good, but training to use the database may be inadequate.  
-We used to have a nice page for search functions--could search any word in ONADE reviews. This is gone now; has been replaced with something newer that doesn't seem to be working yet.  
-Knowing it's there, and then realizing you could ask for it.  
-People that set up these things are not the people that use it.  
-There are territoriality issues when it comes to data. People are afraid of releasing their data because somebody might misuse it. Databases are not shared. No data sharing. Industry would not tolerate this. It's a real problem. You have to go to people and tell them why it would be good for them to share their data. The culture is wrong.  
-Drug data are never public. Our data are not available, we make decisions, and we publish summary of the data. Everybody can see the summary, but it doesn't mean they own the underlying data.  
-We treat our pre-approval stuff in [REDACTED] as proprietary, so we won't even admit to you that we are looking at it unless we have a confidentiality agreement with you.

## 2a. Is there a reason for different safety assessment approaches/methodology between regulatory agencies?

- Partly exposure-driven. Sometimes politics drive unreasonable differences (e.g., Delaney clause).
- Different regulatory mandates between agencies.
- EPA has different ways of doing things/different software. They focus more on contact, inhalation exposure. It differs by what you are looking at.
- There is so little engagement at the staff level with other agencies that it is hard to tell.
- No, hope not, essential that regulatory issues are harmonized for risk assessments. Safety assessment approaches and methodologies should not be different from each other. Should be one standard otherwise you cannot evaluate.
- There is always some reason, such as different weight given to nonclinical versus clinical data (CDER, CDRH, CBER), exposure differences between chemicals, drugs, residues, devices, and for some Centers the risk – benefit assessment
- Historical accidents
- The whole paradigm is different. FDA looks at food risk - safe eaten whereas EPA looks at environmental risk - poison. When FDA looks at risk they look at something that is safe when eaten versus EPA which looks at something that is harmful or poisonous, meant to kill.
- They may have a different set of rules for using safety factors and they usually explain those. Most people understand what the other groups have done even if they end up numbers might be different. I'm not sure there are hugely different approaches unless the regulatory setting is different. As long as you understand the regulatory context and the legal context and the setting I think most of the scientists would understand it. I think some managers get confused sometimes it is not explained to them well. We don't do a good job of communicating what we do and the public certainly can get very confused with different numbers coming out of different agencies.

## 2b. Could it be possible to harmonize safety assessment methodology with other agencies to avoid confusion?

[REDACTED]: To some extent. It depends on what you are looking at (e.g., FA put into the food vs. pesticide as a contaminant). Could not be harmonized completely because they are looking at different things for different reasons.

-Need to ask why do we need to harmonize?

-Doubt it. Driven by the law. Have harmonized data gathering between the U.S. and EU; moving closer to a central data set, but then go in separate directions from there.

-Not at the lower levels. At higher levels, there are the same goals and should be supported the same. Can't always harmonize what you're asking for (e.g., tox data for animals dosed by gavage or in the blood cannot substitute for animals receiving material by ingestion, "at use").

-It would be really difficult. Harmonization is important from a consumer advocacy group stand-point and it is difficult for them to understand why it is not done.

-Not always possible to standardize everything. Could make processes more transparent so it doesn't look as if different agencies are doing things differently capriciously.

-It may be possible to harmonize some portion of our safety assessments. EPA looks at the same stuff that we do and so we should have a similar approach to calculating exposures.

-No, the basic tenants of risk assessment and safety assessment may be the same but difficult to harmonize because the end result is different. We are looking at two different aspects of a given ingredient.

[REDACTED]:

-Don't think it's possible due to the risk/benefit ratio being driven by medical needs for pharmaceuticals, devices, and such.

-Timing dictated by regulations is another constraint. It might theoretically be possible to have the front end tox assessment be consistent and then incorporate the risk/benefit analysis at the tail end but there would still be the issues of other centers being able to have human test data, require any data they seek, and consider other factors that we can't.

-We can agree on certain ways of doing risk assessments. But the end might be totally different reasoning in terms of whether each deems it safe or not safe.

-This has been tried (Health Canada and some South American Countries), but could not reach a consensus on how to harmonize, due to different consumption levels, use of different safety data, etc.

-In some cases it's possible. (b) (5) approaches are congressionally mandated. FDA could choose to follow what (b) (5) has been mandated to do, but FDA is really science-based. If it doesn't seem like the best science approach then they wouldn't be inclined to do just what (b) (5) is doing.

-They have worked hard at harmonization but has gone nowhere. It has improved in understanding one another and communication. This is the current trend: FDA/USDA with EU, Health Canada, and other countries. Interviewee is working with Asian countries (China, Japan, Korea, Thailand, and India). WTO has different standards. Scientifically we say why not but not practical.

-We do have some level of standardization. The methodologies used to conduct the various types of testing are standardized. E.g., EPA does a genetic toxicity evaluation of a pesticide or a metabolite from a pesticide, they follow standard protocols. They have changed the names to "benchmark doses". (b) (5)

[REDACTED]:

-To some extent they are already harmonized. We are using similar methodology. The difference comes on how it is applied to the product that is being assessed, reviewed, or approved.

-Don't see a need. We would not regulate our food chemicals the same way pesticides are regulated. We have harmonized our guidelines for reproduction and teratology testing with the EPA guidelines. So if the exposure is high enough then we would recommend a reproduction study then the notifier could use either EPA's guidance or FDA's Redbook guidance. If it's a non-pesticide chemical, it may be regulated by EPA and FDA as well. Reproduction and teratology testing were harmonized with EPA - OECD - FDA guidelines.

[REDACTED]:

Think it could. International Conference on Harmonisation (ICH) is the global attempt I see for CDER, CBER, and CDRH. Not sure if OF (CFSAN & [REDACTED]) plans to work with EFSA or OECD and other countries toward a similar ICH standard?

-Yes, we should go do it and check out what EPA does. In many ways it would probably be applicable to what we

do. If we get rid of Delaney.

████████:

Yes. In collaboration with USDA and CDC, have seen the benefit of using market sales data with label data. We are all working on that but there is a matter of resources. For a lot of these databases they want to sell it three times to each of us, instead of one big packet. In general it can be harmonized, especially with a math background you can talk in coding and programming to each other.

████████:

████████ is currently moving towards EPA methods (MOE, benchmark dose, point of departure) but has no Guidance or statutory basis from which to proceed. Regulations are still based on ADIs, NOEL, and safety factors. As indicated under "Science Issues" harmonization of "assessment methodology" is practically the same as comparison of Evaluation Methods. This question can be answered by direct comparison of SOPs / Guidance and perhaps selected reviews between groups. Harmonization is useful only if the process answers the same questions and provides useful answers.

████████:

-Yes, where it fits. When they updated Redbook, they looked at EPA and OECD guidelines to see what they could use.

-Don't think it would be possible to harmonize methodology across agencies because each industry gets used to the agency they work with. Not sure it can be harmonized within FDA, but would be nice to try between Centers.

-Although there are many instances they can harmonize even at the international level. The International Council/Congress of Harmonization (ICH) works with certain types of testing to harmonize- to create one uniform standard for toxicity testing. Those mechanisms are out there.

-It is a must, but how practical it is he does not know. Science should all be on the same page. Otherwise how can we evaluate.

████████:

Maybe yes for some aspects. The work is based on different assumptions within the EPA and FDA, but the rationale has been lost.

-If the Foods Program agrees that Tox-21 is the best way to achieve our goals there needs to be broader participation. However, given the small size of the Foods program relative to other participants (e.g. the EPA Office of Pesticides has as many employees as all of CFSAN) we may not have the resources to be influential, which is why perhaps creating food-specific project committees may be a better route.

-Part of the confusion is that people keep trying to harmonize things that shouldn't be harmonized. That gets people really confused. Need to separate the science from the policy. Harmonizing policy may be necessary but you need to make sure it's a policy question. Harmonizing science is to some extent anti-scientific because you need controversy for scientific progress.

████████:

-Can be done to some extent. Tox endpoints should be consistent. How you interpret the data will be different and depends on the reviewer.

-We typically do that and we have an FDA guidance document that talks to that. There are documents on risk assessment describing the framework and the steps. All using the same framework but approaching from the direction our particular risk or hazards come from.

████████:

-There is a reason for them to be different, but if some common tool is used (e.g., risk assessment), there should be familiarity/common with how to use it or understanding of it. Any departures should be made for good reason. If you do a harmonized answer, then you are not tailoring your answer to the product.

-Both Centers do ADI (CVM) or a similar assessment at CFSAN (TDI or EDI?), which is similar to that done by JECFA. CVM is trying to harmonize with JECFA, so it seems as if it should be possible within the Agency or the U.S. Could be similar, but there are limits

-Could be similar processes/steps, but they are different programs for a reason. There can be consistencies without everything being exactly the same.

-Everyone applies the same principles, but in detailed approach, it may not be possible because of different compounds and regulations. Possible at a higher level: harmonize for drug approval with EU and Japan, but this is for animal drug. But we cannot harmonize with ██████████ because they do not use VICH guidelines. Possible for same

kind of substances.

-Science can be harmonized. Regulatory mission/practice needs to be specific to the mission.

-Believes more could be done in terms of harmonizing the information that is being yielded by the new technology, which does not fall under outdated guidances (e.g., coordination of nanotechnology work groups across the Centers).

-So what I see internationally in food organizations is a great many organizations will come up with the same ADI, that's a very non-derivative answer. They often look at the same studies. Once you have an ADI it gets played with and gets changed into other numbers. We routinely find there are differences in what the U.S. does for the residue mitigation part of an evaluation. It's different from what Codex does, what the EU does, and what Japan does. Everyone has a reason. Maybe having internationally harmonized guidances is going to be the jump start to all of this. Certainly the toxicology guidances that have come out of VICH may drive any differences in ADI setting to really come together and make it be a fairly unified process.

-Think for some the methodology could be harmonized. Should develop a strategy based on scope, exposure, and chemical.

-Yes, should think so. In my work, we coordinate with Food Safety Inspection Service (FSIS) which is part of USDA. They are involved with the monitoring aspects of tissue residues of drugs.

[REDACTED]:

-In broad strokes risk assessment methodology is exactly the same everywhere. It identifies hazards, it looks at exposure pathways, it estimates risks, and then it talks about uncertainties. As long as you are not doing a checkbook everything is completely harmonized. The minute you get that stinking checklist out you're done.

-Changing regulations this day in age is nearly impossible. It's even impossible to get a guidance out. We need a more flexible way to do that including doing some minor changes to regulations that say, "as appropriate". If you could insert the phrase "as appropriate" in a few places you could give yourself the flexibility to look at different data sets in different ways.

## 2c. If so, what ideas do you have to reach this goal?

Talking: informal or informal discussions. But it is difficult because they have completely different perspectives, terminology (e.g. workshop with EPA on different sub-populations).

- Would require a lot of communication: two programs both think they're right, so have to go one way or the other or compromise. Needs to be thought out carefully for resolution.

More meetings. Would need someone who understands both sides with good vision.

[REDACTED]:

Can do more--when it makes sense. More communication/interaction. Relationships with EU (continuing) and Health Canada (b) (5) to discuss food contact regs.

-It is more important to explain the differences and why they're necessary than it is to harmonize methods. From the Pew Report came the issue of perception vs. transparency. For harmonization of exposure and toxicology data, people don't understand why we are asking for different things. Need to educate consumers more; provide better outreach.

-Collaboration - working with other groups (EPA) in assessing those chemicals involved. They are doing this with the pesticides group at EPA looking at antimicrobials.

[REDACTED]:

-Look at each other's protocols to see where they might be combined.

-FDA could do better: better data harvesting by requiring more data, but industry says they can't do this.

From their perspective, the more data they provide, the more it slows down the process, so industry is not likely to submit more data. Need to explain the government risk assessment process to consumers and get their feedback on what they're willing to pay for this.

-Harmonization could only be achieved at a very high level of government; not at the staff level.

-EPA has the resources to do these very extensive risk assessments; often these risk assessments are in chemicals that are of interest to the FDA as well. If FDA and EPA could set up a situation where FDA scientists or regulators could participate in that EPA review in some way, then FDA could rely on these reviews and have confidence that FDA needs were being met in that review as well. FDA does not have these resources (personnel or time) to do the risk assessments that EPA does.

-If other Agencies or Centers have information that we don't have or are not aware it even exists then it is possible that they might be deciding their safety decision on information that we don't know and so therefore there would be a different outcome.

[REDACTED]:

-First we need to convince management and lawyers that they agree to that. This has happened three times before that people tried to change the Agency's perspective on secondary mechanism and every time it was shot down and it didn't go anywhere. It is scientifically incorrect and still didn't go anywhere. If that happens over again, the scientists on the outside will declare that the science on the inside as limited and wrong when it comes to an outcome of an assessment that doesn't integrate these newer, by now almost outdated, approaches to safety assessment.

[REDACTED]:

-The data analysis group for safety assessment from each Agency should discuss every quarter and that should be made a priority

[REDACTED]:

-It would take a commitment of time and resources by the highest level of management in all the Agencies involved. There have been efforts at the level of the risk assessors to try to communicate between the Agencies but that is limited because of the different regulatory authorities, different cultures in the different Agencies, and the short-term focus of the political people who often appointed to run the Agencies.

[REDACTED]:

Can do a better job. Make efforts to have access to high throughput data as a baseline for us. Use with established methods plus these in a step-wise progression.

-Need to get to more meetings (now ~1/yr). Need to choose between science and regulatory meetings. This is where you get the most information in the shortest time.

-Try to have money available when the need arises, rather than more money.

-Need to send the right people to the meetings; not the same person going over and over.

-Has to happen in Congress, if statutory.

-Does not know at his level, some committee or upper management decision. DOE and EPA harmonize risk assessments, believes it is there but not sure.

-You need someone with clout heading the group. It has to happen at the top (White House).

[REDACTED]:

Go through the methodologies and re-assess to determine if differences are really appropriate.

There is a difficult balance with ongoing work. It is limited by resources. Now prioritizing “mission critical” projects, so emerging issues get moved down the ladder. This is all right for now, but could become a problem in the future. There is a difficult balance with ongoing work. It is limited by resources. Now prioritizing “mission critical” projects, so emerging issues get moved down the ladder. This is all right for now, but could become a problem in the future.

[REDACTED]:

-IRAC is a good example (Interagency Risk Assessment Consortium)

[REDACTED]:

-Cross-training, joint working groups/committees (JECFA model) would help this. Need to get the groups talking more.

-If there are meetings to address these issues, need to have the people in the room who can make the decisions.

[REDACTED] tends to be isolated from this procedure because it is not located at CFSAN.

-Ask why/how they do something one way and then can apply to a different situation. This might allow tailoring to fit the exact endpoint that a group is looking for.

-We need to do a lot better job at letting the public know that science doesn't get you to one number agreed upon by everybody.

-Think we need to find ways that all this information is readily shareable in real time; important to keep the flexibility in there.

-Look into the background and find the scope, what are we looking for in terms of risk assessment. What are the scope, goals, and objective of the study before reaching out? Then have a discussion if it can be done or not.

More coordination. Good example is when [REDACTED] set up the GRAS program we went to CFSAN.

-Having people switch chairs. Have them visit for 30 or 60 days to see how we do it. Have meetings where several topics could be presented. We had started doing this when we were considering food contact notification for DAF. We didn't go there eventually but did have a couple of presentations.

**3a. At what levels and in what manner does the program interact on significant chemical safety and risk assessment issues with NIEHS, CDC, EPA, USDA, other federal agencies, and international bodies?**

Have worked with CDC (trans fats), USDA (often due to overlap of regulations, when we have to), internationally (recently started communications with EFSA; there is a liaison here; can share their exposure data)

████████:

- In cases where there were different safety decision on a some products (e.g., JECFA or EFSA vs. FDA): If their position was more relaxed (EFSA), reviewer was urged to accommodate theirs, even if we had legitimate reasons for rejection. When their decision was stricter (JECFA), reviewer was urged to stick with FDA's decision.
- Close relationships with USDA (processing plant materials); liaison CSO to coordinate submissions. Transferred antimicrobials to EPA; working with them on review of principles, chemical reviews, assessment. Working with NIST on nanotech - inter-agency nanotech working group.
- At regulatory level, not at all with Federal agencies, but if anything, more with international bodies. One example was an EPA seminar that was great.
- On the whole effective, bit affected by priorities: may receive a rush assignment; therefore, a good review is difficult. E.g., WTO (World Trade Organization) notifications from USDA; sometimes turn-around is not long enough. This issue can be addressed in a number of ways (general mailbox, etc.)
- We interact at all levels with respect to these agencies when you have significant chemical safety risk assessment issues. We have had various meetings through the Advisory Committee to the Science Board at FDA. We have someone from the European Food Safety Authority (EFSA) working at FDA. We are working with them but they all have specific rules and regulations and we have to work within the confines of our own rules. We cannot let one country dictate what we do and we cannot dictate to another country what needs to be done. We have to abide by our own rules.
- We have a regulatory framework (EPA, USDA, and FDA) to regulate crops. OECD International task force which looks at the composition of novel foods and feed. JEFCA (independent body), WHO, FAO - ask for expertise within the Agency for a food additive or a contaminant/impurity in food.
- There is not a lot of it, but when we do, have points of contact within USDA, EPA, CVM, so if there is a cross-cutting issue, we how to get people involved (e.g., USDA on meat and poultry).

████████:

- Collaborate with USDA on microbial washes of poultry.
- Otherwise, as needed for special cases. This seems to work better at a higher level.
- Some involvement with EFSA and WHO.
- Some designated people do this. Currently, it is on a case-by-case basis and person-to-person; selected by management.
- Not as much as we should. NIEHS and CDC do not have any statutory mandate to perform formal quantitative risk assessments or safety assessments that we do. This makes the interaction somewhat strained, in that they would like to do these risk assessments but do not really have the expertise. EPA and USDA do have mandates, but we did more with them in the past.
- Works with CDC: Na reduction. USDA: food ingredients safety assessment vs. suitability assessment, MOU for information procedures. EPA: biotechnology; exchange of information and technology.
- We frequently interact with NIEHS through the National Toxicology Program (NTP) because we have an interagency agreement with them. EPA - liaisons for questions, have cross-cutting issues, antimicrobials on environmental exposure issues, and regulation. USDA - we interact with them but not with toxicology. Have contacted colleagues there on the safety of nanomaterials. EFSA - MOU: we have started to exchange confidential information on products that we may be reviewing for safety at the same time they are reviewing the same product. USDA - sometimes we interact with them when our additives or chemicals involve meat or poultry applications; with NIEHS (NTP falls under this) we interact with them regarding carcinogenicity data studies, we may be asked sometimes to recommend potential compounds they might test; ICCVAM - we interact with them; it's a consortium of several agencies including EPA and NCTR. It's a validation of study methodologies. We also interact with WHO, JECFA - some of our scientists participate in individual, independent, safety review assessments. We interact with the European Union, EFSA - sometimes we share reviews.
- When necessary and when regulations and law demand, do collaborate with other agencies and divisions (e.g., use in food and meat requires that we work with USDA).

■ :  
Informal interactions between reviewers appear to work well for discussion of issues and ideas  
Interaction for actions on risk assessment issues work well when higher level management authorizes and dedicate appropriate resources. FDA provides relevant experts to international regulatory meeting (e.g., WHO) which is useful for supporting regulatory science and standards in assessments. FDA collaborates effectively through scientific review meetings with intramural NIEHS/NTP programs.

■ :  
-FDA and the CDC have reviewed proposed rulemaking with the USDA on bovine spongiform encephalopathy (BSE) and international classification (OIE) of countries on BSE risk (negligible, controlled, or undetermined). We have adopted some guidelines from EPA on thyroid cancer risk assessment, at least pathology but haven't gone further.  
-We have telephone conversations with them on issues [BPA, 4MEI (caramel color; (b) (4))] but their methodologies are very different. Thresholding, EFSA thresholds everything (carcinogens, any toxicological issue) and we don't do that because we still operate under Delaney.

■ :  
We have done document review for EPA, CDC, WHO, so we do interact quite a bit. The system works pretty well. Work in contaminants is sporadic, so the group may get overloaded.  
-There seems to be virtually no connection to EPA or USDA at the staff level. Up to now FDA has been very influential in JECFA although with (b) (6) retirement the contaminant side of that relationship may need some attention. Participation with IARC seems non-existent; OECD participation is very spotty and not well supported. There are tentative steps to engage with EFSA but the structures of EFSA and FDA are so different that it will be a real challenge to interact with them. There are some staff to staff contacts between individuals in CFSAN and EPA and NIEHS but with the exception of BPA these are mostly uncoordinated with CFSAN leadership.  
- We have interacted with EPA over the years but at times we are at odds with EPA. They set standards that people think should intentionally or unintentionally be applied to food. But there are other issues they need to think about. With USDA and WHO we are all working on food and so we do not have that same issue. We have collaborated with WHO forever. We are starting to collaborate with USDA. Before we were the USDA toxicologists but now they have their own toxicologists.

■ :  
■ and above interaction; not branch scientists; implementation of Tox21 is well underway as a result of this higher level interaction.  
-Not sure we're doing a good job at this. Good to be transparent and some of the Agencies are involved with food. Globally some international bodies that could be involved EU – cosmetics (no interaction/closed box). Some interaction with Canada-Japan-EU for cosmetic. Haven't interacted directly on a Chemical Health Risk Assessment.  
-With some of them we have liaisons to different programs: our new ■ is a liaison with NIEHS program, ■, lead toxicologist, is a point person with many national and some international programs.  
-Tox 21 working committee so there are interactions with NIEHS, NTP, and EPA on those issues.  
We frequently work with CDC at our laboratories as well as USDA.  
Internationally we have representatives that do work on harmonization guidelines and guidances.

■ :  
We have a liaison to all of these agencies, but we are unlikely to get them involved in our decisions before we make them.  
-We may invite comments, but provide such a short turn-around that it is not very effective.  
■ :  
■ : International = Codex, JECFA, SPS (Sanitary Phytosanitary Trade Agreement), WTO ( and USTR), USDA Foreign Agriculture Service (FAS): daily/weekly access.  
-NIEHS (NTP): interaction on databases, products. CDC: antimicrobials monitoring NARMS/NAHMS progress.  
-NEPA: Every veterinary drug or food additive undergoes NEPA evaluation. EPA: as needed on food safety reviews; have shared data packages with EPA.  
- His team makes jurisdiction decisions: decide if the article is a drug vs. pesticide (EPA) vs. animal biologic

(USDA). Interact with CDC (panels). Do these kind of interactions routinely. None with NIEHS. Also [REDACTED] (genetically engineered animals and fish) interacts with Federal agencies and at least two other countries. Depends on the issue/article.

-The Agency asks for those who are interested, then assigns whoever is available. Becomes a Black Box Operation

-The Office of Translational Programs within FDA works as a liaison between Centers and facilitates contact.

-Doesn't think they do; maybe in a national crisis they do.

-Well coordinated. He has interacted with USDA and FARAD. This has been self-initiated, which is very good. Have consulted on research projects with USDA in ND and it worked out really well.

-We are harmonizing our guidelines internationally with organizations including WHO. Work with USDA on tissue residue monitoring, toxicology staff work with EPA, NIEHS on specific topics

There are many meetings (with team leaders, management) with USDA, CDC, EPA, and internationally. We are kept up to date.

-We interact a lot with JECFA, Codex, OIE (WHO). USDA the residue team interacts more than the tox team, especially on vaccines. EPA, some on Tox 21. Also MOUs with Canada, EU (?), and USDA and Canada. There is an Interagency Toxicological Safety Assessment Committee with NIEHS, NCTR, and FDA. We have interactions on significant issues.

-With USDA and EPA, we have an across the agency working group that meets once/month to talk about drug and pesticide residues in agricultural products. It covers more than meat, milk, eggs, and honey; that's what we focus on when we're together. CDC works with us on antimicrobial resistance and residues in food that are antimicrobial residues.

-There are some interagency groups that are working together to validate analytical methods or alternative methods.

-Example: One time we did afford ourselves to coordination and collaboration on cross cutting issues was the Fukushima incident in Japan where we talked to Offices in USDA on a regular basis and other like individuals at universities and foreign governments. It was stellar indicator of lack of impediment.

### 3b. What has worked well in this regard?

#### Special issues

- National Children's Study-epidemiology-there was interaction with all Agencies
- Good interaction with USDA (FSIS), EPA, CVM on the risk assessment for cyanuric acid and melamine. Generated a risk assessment document reflecting review by all. This does not happen routinely. Is it necessary? What will be gained?
- FSMA (Food Safety Modernization Act) food allergy issues in schools, works with CDC; has worked well.
- Generally these interactions occur when we are working on the same issues, so it's helpful to get different input.
- Tox21
- joint group with FDA, CDC, and USDA working on food borne illness attribution, BSE, where we extensively interacted with USDA on that.
- No problem with interacting with international bodies as far as our safety reviews are concerned. We rely on them and they rely on us, particularly EFSA. They have a feed additive cluster here now and so we interact with them. The States do a lot of work for us. They do investigational work with respect to medicated feed mills. Our group would probably only interface with the Association of American Feed Control Officials and State Officials with respect to any risk assessment issues.

#### Training

- ██████████ brings back current information on trends and what's going on in the field of toxicology faster than what we would pick up in the normal literature or publication channels.

#### Methods developt.

- ICCVAM - we interact with them; it's a consortium of several agencies including EPA and NCTR. It's a validation of study methodologies
- Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) validating alternative methods - USDA, EPA, DOD, FDA.
- As far as my experience is concerned, the link up or collaboration with FSIS for method tryouts. It's optional for them.

#### Standards/Policy

- Interagency working groups. Also, international groups: JECFA, Codex, EFSA. Exchange goes both ways.
- EFSA has regular meetings to discuss core issues. Works well with a body where you are sharing a lot of information. For EPA and USDA, is more situational
- Internationally (recently started communications with EFSA; there is a liaison here; can share their exposure data)
- The goal with collaborating with WHO is setting international standards. USDA, works with CVM too, to get common approaches to regulate contaminants.
- EFSA - the EU has a resident representative that we can use to communicate with EFSA. EPA and USDA - talk to them when we need to on common issues regarding regulation, not safety.
  - ██████████:
  - The participation in the formal international bodies has worked well.
  - ██████████:
  - Our participation in international committees to develop harmonizations. Codex has worked very well. We have had a lot of successes and put out guidances that were harmonized.
  - ██████████:
  - Worked well with EPA in establishing an import tolerance program, but it would have been nice to have a good contact at EPA to talk it over with.
  - Harmonizing of data requirements on an international basis (with VICH, Codex, JECFA).
  - EPA brought us together quite nicely. These informal where we present our risk assessments and get input and feedback is very helpful. The development of policy and doing it across the Federal government for an EPA initiative for the microbial risk assessment framework got us together on a regular basis.
  - When it comes to international bodies, Codex, we coordinate well.

## Other

Even at the staff level, can be involved in experimental design to get needed information. Interagency working groups. Also, international groups: JECFA, Codex, EFSA. Exchange goes both ways.

-They do work well: saves resources, can leverage reviews that have already been done elsewhere. Gives us more information that we can use without going back to a petitioner, etc.

- Can help with a review, when an international body has already reviewed data for a product: do we agree with what the reviewed and how they reviewed it or not? Institutional knowledge gained from working with other organizations may be applied.

-Staff exchange

-Document review

-Some feel international connection is not in line with the mission, but it is because we need to represent the U.S. in international trade.

[REDACTED]:

-Recently a person from the European food administration came over to U.S. for a 6-month detail. There is a good collaboration.

[REDACTED]:

-On risk assessment issues, that works well when the higher level management authorizing can dedicate the appropriate resources. Risk assessment requires the engagement of higher level management.

[REDACTED]:

-Coming to the table with an open mind. USDA has a slightly different mission than FDA. EPA is in the middle. Listen to what other people are doing and what they are concerned with. Being respectful, be open, and push back if necessary.

### 3c. What improvements are needed?

#### Communication

More clear lines of communication.

- Keep talking with them; open communications.

[REDACTED]:

-The more interactions you have, the more comfortable you are exchanging information. Sometimes the process is overly formal.

[REDACTED]:

-I'm not even sure that we know what list of chemicals EPA is working on at any moment, or USDA, or the others

-The communication could be improved. We need to receive some information from NTP(b) (5)

[REDACTED] on us; they should have given us a heads start so we could ready our responses, rather than see it come out in the press first. Communication with EFSA is new and is sometimes fragmented. Their responses are not in a timely manner.

[REDACTED]:

-There have been issues with specific additives and discussing the chemical safety of something with EPA and USDA. EPA is looking at pesticides and has a totally different reason for looking and so we have to be doing things differently. There is nothing wrong with that but we need to be communicating well to outside world that this is the way EPA does something their way and this is why we do something our way. It's the same but it is not.

[REDACTED]:

Large organizations, but maybe committees could be set up, rather than just working committees in response to a specific issue. If something were relevant to our procedures, we could communicate results back, seminars, etc.

-Technology (teleconferencing, e-mail) could be utilized more to improve communication, even informally.

-Communicate better with other organizations; pass information (relevant ruling/decision) down to reviewers.

#### Support from top

-For international meetings: Perspective: some feel international connection is not in line with the mission, but it is because we need to represent the U.S. in international trade.

-A commitment of our senior management for time and resources devoted to the job. Take a long term integrated point of view as opposed to short-term immediate problem solving.

-Proper dedication of resources. Supporting people that have to do work in these interactions. Provide the proper messaging of our needs and actions.

- One doesn't know enough of what is going on in the other Centers. For that kind of coordination they need resources. If it were formalized there would be official resources to fund it.

#### Better data sharing

More data-sharing agreements.

[REDACTED]:

-Possibly, cost savings could be had by having better access to safety assessments done by other agencies, but we are reticent about picking up anyone else's safety assessments.

-We don't interact well with EPA. Example: We both had concurrent issues with [REDACTED] (b) (5). We asked EPA for some confidential information they received on [REDACTED] (b) (5) data and they flat out refused to give it to us. Even though these were just contaminants. [REDACTED] (b) (5).

[REDACTED]:

Committee(s) that are liaison committee. Could review documents before they have been completed and identify who outside the agency should/would provide comments on them.

[REDACTED]:

Proprietary issues are a problem, but can be worked around. They are working to set up confidentiality agreements with Canada (VMA, VDV, CFIA and others) so that we can share data: quarterly meetings, RCC program to coordinate with Canada on vet drugs.

[REDACTED]:

-Think that OSTP or somebody or some entity outside a specific that cross USG needs to spend some time thinking about how to protect CBI on one hand and on the other hand execute a series of MOU among agencies so that we

can share data and information in a way that lets us make the best science-based decisions and to ensure that risk mitigation is handled in an efficient effective way.

### **ID relevant staff**

- More clear guidelines on when to contact.
- Ideally more of this can and should be done by new people who are more current with new science. All levels should be involved
- Having a contact person. You can lose your contact person when staff changes. Maintaining this contact person information is not a priority for either agency, but should be.
- Don't know who to talk to at different agencies; don't have an established way to do this.
- Some way of identifying risk assessment personnel in other agencies and vice-versa. Often your supervisor may know someone and send an e-mail for you, but there might be no follow-up.
- Communication: the contacts may change within an agency and you don't know.

### **Staff exchange**

-Consider a 6-month exchange of staff with EPA or USDA in applicable areas. Increase communication. If this is of interest to the Agency, someone at the executive level should define areas of interest for collaboration and who at the other Agencies we should collaborate with, and then organize it. Can't come from the lower levels.

### **Dispute arbitration**

Establish a mechanism for arbitrating disagreements between agencies.

### **Other**

- :  
-All reviewers should have exposure opportunities. Right now only a select few get this exposure. In some of these cases it's management chosen but in other cases it's voluntary. Would be helpful for all.
- :  
-Our doing things as they do is limited by the fact that we just don't do it like they do it because we still have Delaney. As soon as someone says we do not have to consider Delaney anymore, we can threshold, we are at the same scientific level as they are.
- :  
-Certain issues always go to certain people. Need to open up opportunities for different people to become involved. Timely interaction. Bad idea to impose your way of doing things on other people.

### 3d. And how can we best achieve these improvements?

[REDACTED]:

Hire more people, we need more resources. Nice if people were doing only this. There are always competing priorities that have to be juggled with “bread & butter” work.

[REDACTED]:

-Participate in other Agency meetings as a passenger to represent FDA. Should be done more.

[REDACTED]:

The Senior Science Advisor staff and the relevant offices need to continue their efforts to develop ways to create and communicate priorities. There also needs to be a method that allocates resources (time and travel) once priorities are identified. There are so few toxicologists in program offices other than [REDACTED] that it is easy for long range priorities to become secondary to immediate needs outside of toxicology when budgets are tight.

[REDACTED]:

We have made extraordinary efforts to be at the table with other groups on vet drugs. There is a very active International Programs Team (IPT) in the Center.

-As an example, consider the number of agencies a company needs to contact for one substance (e.g. food additive algae for animal foods: EPA, FDA, USDA, APHIS, trade office, etc.). Not sure how to fix

-It's historical; what they do, what we do. If you're going to talk about it means that you are going to have to change the way somebody is going to do it.

-An agenda helps.

**4a. What is the current state of scientific transparency and engagement internally and between FDA's chemical safety scientists and programs and the external scientific community?**

**Internal**

-Good; feels there is access to any information that is needed internally on any safety issue. Only problem is finding older information.

-Some decision-making processes are not clear in-house.

(e.g., BPA (b) (5)

ut the in vivo studies did not indicate estrogenic effects

-Internal: all memos are available to anyone in CFSAN. Difficult to find who does what within different buildings within CFSAN; no organizational directory any more.

Internally it is OK. Attended a good meeting on food safety research at White Oak that was good/informative. Databases like CARTS help track research. Within [REDACTED] they have weekly chemistry meetings to discuss what is new in each division. This is excellent for communication. Invite chemists from ORSA to come and share their information, and it is useful.

-Internally within our Office we are very transparent.

-It's pretty transparent, but finding information is difficult still. Even within the Agency it can be difficult. It can change every few years about who the contact person is, where to find something, and who's who supervisor.

Periodically they have put together a resource list of expertise, but as a reviewer I have never seen that list. When I came in I got a list of experts, but probably 90% of those people are gone. Feel there have been efforts to update the list but I have never seen one.

-Internally, there are issues of collaboration. There seems to be competition between NCTR and the toxicology group here. Research feels as if it is 2<sup>nd</sup> fiddle to NCTR. (b) (5)

-Internally: sometimes not very transparent. E.g., For attainment of instrumentation or materials, information is spread by word of mouth. Not much sharing. Information is provided on an as-needed basis or as they want to. The division was reorganized with little notice, explanation, or buy-in by the group.

-Not transparent; we find out after the fact. We are not allowed any input.

-Internal: could be better across Centers for overlapping programs. They are trying. E.g., a certain risk assessment is going between the centers: no intentional lack of transparency, but there are still difficulties.

-Internal: OK in terms of engagement. Within [REDACTED] different areas may consult with each other (companion animals would consult with human food safety before approving a drug).

-Internally: a lot, if you ask. Questions are answered openly.

Working on it: more focus groups on similar products, even if it's not directly tied into their area of expertise.

-Internal: not very across Centers or divisions. For some: this is our review, this is how we wrote it and that's final. Reviews are not made public to other groups.

-There is a general lack of transparency. We don't have time because we are chased by deadlines. Internal: most people don't know what other centers are doing unless they're on committees.

-It happens on a case-by-case basis, once in a while, but not on a regular interval.

## External

All memos are accessible through FOI, but that doesn't make them easy to get.

Real-time interaction with the external scientific community can be tricky.

-Externally, have made attempts: Pugh, webinars (trans fats), seminars, international meetings, poster at ACS; does not always occur on the time-frame required by external community.

[REDACTED]:

-Within the Center, not everyone knows what each Office is doing and so this causes communication issues with the general public. One office might be finding one thing on a specific topic and another office might have contradictory findings and so this leads to a bad public impression.

External: via FOIA. Trying to post as much information as possible on the web site to try to circumvent FOIA requests. Looking into what can be put on the web-site (after redacting proprietary information).

-Most of the environmental decisions and supporting memoranda are already available.

Externally- Not so great. Within [REDACTED] (b) (6) division, it is difficult to publish results (may take 6 months to a year); it's even difficult to get posters through. ORSA does publish, and it is great.

-We have the information available (e.g., guidance documents, the website), but it is very difficult to get to/find. It is written from a very scientific standpoint, but not very public or consumer-friendly.

-We are working within our Office to make more of our reviewed memoranda (chemistry, toxicology) available by the click of a button and putting it on web pages. Our GRAS review group has put a lot of their memos and letters on the website; we are also looking at doing this for other documents. Working on being more transparent.

-We are not transparent enough to the public and this leads to mistrust.

-Looking at biotechnology there was an urge of transparency from the beginning of that process and so when we write notes to file they are very long because all the amino acids are listed out individually. There needs to be a balance between that and reasonable transparency. We could get more out if were more concise, but there has to be an agreement between all parties.

-Externally - transparency with the scientific community but there is not enough transparency with the non-scientific community. Don't know if the non-scientists are hearing the science-based policies that FDA has.

[REDACTED]:

-When things get blown out of proportion, cannot always react properly (e.g., BPA may come off the market, but we know little about the alternatives, and they may be worse in terms of endocrine disruption).

-I believe that, in our office at least, it is viewed as unacceptable to ask questions at open scientific meetings or make personal statements about one's scientific views for fear of giving someone in Industry or the Advocacy arena ammo to bash FDA.

Adequate: Anyone can FOIA information.

-CFSAN is not transparent, which has created a serious breach with the external scientific community and the public. This is a great hindrance to our credibility. Openness makes us vulnerable, which tends to be avoided if at all possible. Denial is the most common defense, as if publication of final regulations in the Federal Register meets the criteria for transparency. It does not by a long shot.

[REDACTED] (b) (6) issue is with industry coming to FDA for pre-market meetings: they are not very transparent with us; withhold information. Need to develop a rapport with industry. Clarify what the requirements are and that we are willing to work with them. Help with study design, protocol. Industry wants info from FDA but doesn't want to give up information; don't want negative information to be released; not forth-coming with data.

-This is a contentious issue. FDA's science is robust, but the scientific community doesn't understand the regulatory side of science.

-Transparency is very good when FDA has completed its assessments. During the process there is not a lot of engagement with the external scientific community. This is poorly perceived and could be improved.

They can request data through FOIA. We publish in the Federal Register (FR), but not sure the public or a lot of the scientific community understands that the FR exists and it is not a good way to understand how we do a review.

What we take into account. What types of back up and checks do we do on our own reviews? We need to find a better way to communicate with the outside world.

[REDACTED]:

With the external scientific community, there are two groups. 1. Groups that understand the regulatory scientific process seems to have better and more productive interactions with the FDA. 2. Groups that expect FDA to regulate on the "precautionary principle" or on science with high uncertainty have difficulty in FDA interactions.

The current level of engagement is strained with certain external groups. The lack of objectivity and focus on one's own research outside the context of other research in that scientist's field can prevent constructive engagement with FDA. Another self-serving interest that can obstruct productive engagement is the desire to have FDA acceptance

(or validation) of certain research to help build funding for a topic, lab, or institute.

\_\_\_\_\_:  
-It's not very transparent. Part of that is because of the nature of how the Agency thinks of itself as a regulatory policy agency and the restrictions that it places on being transparent. That is not an issue for scientists so much as a broader policy (legal) approach within the structure. It's easy to use those restrictions as an excuse of not doing anything rather than putting in some effort into trying to find ways to do it anyway

\_\_\_\_\_:  
-I do not think it is a good idea to have people intersect the review process at any level. Disclose if asked, that's transparency. Think we do that.

\_\_\_\_\_:  
-There are definitely some transparency issues at least from the math side. For example the math problem work was contracted out and then we could not say how the number was obtained. We just said, "We just used some people to help us get that number." What we could do is show the basic math problem, this is what we did, this is the data we used, here are the assumptions we had to make, and this is the best we could do, and if you have a better way to assist us feel free to.

\_\_\_\_\_:  
The problem is publication. It is not as easy for a regulatory agency as it is for pure science. Another source of problems is that it is difficult to set consistent standards for food because of different population groups, etc.

\_\_\_\_\_:  
Pretty good. Can go to meetings, make posters, presentations.

-Can publish methods.

-Interaction as needed on specific issues.

-You can use connections that you have, if they'll let you. Can set up, but tough to get it past the manager; depends on the individual. Some get more opportunities than others.

-From our standpoint the laboratory safety research is published and puts it out there for the outside community. Not aware of any problems with publication or any attempts of censorship. The Gulf oil spill the publications were slightly delayed because politics were involved, but never seemed to be a gross hindrance of communication.

-We publish our reports in peer review journals and so it is transparent. That is the difference between the research scientist and the reviewer. The reviewer has to go through different layers of approval, but for the scientist our manuscripts are in the public domain.

-We are not allowed to communicate or leak out anything.

-Microbial risk assessment - better degree of scientific transparency and engagement. BPA highlighted problems with transparency.

\_\_\_\_\_:  
Very poor. Both \_\_\_\_\_ and \_\_\_\_\_ don't communicate their decisions as well as they should

-Tend to be reactive instead of proactive. Office of Communication has been trying to address potential issues either before or when something becomes an issue.

\_\_\_\_\_:  
-External: difficult, mainly because of proprietary issues: can't report on submissions until they are approved. Once a decision has been made, try to be very transparent. Publish a FOI Drug Summary with every approval to be issued before there are FOI requests. It is part of the approval process, but is not issued for items that are not approved. Hardly ever say no: send back for more data. Identifies key reports/data, provides a road-map to the decision. Re: CDER Model: They simply issue redacted reviews. (b) (6) feels these are less transparent because they are simply putting forward technical information but with no explanation of the how the decision was made.

-External: Trying as much as possible. Difficult because of the ever-changing policy stance. If we change our minds on things, the perception is that we are not being honest. Better to say we don't have a stance yet, than to create a stance, and then change it.

-We like to think we're transparent because we put out guidances, but if it's new, like nanotechnology, we haven't done very many of them because it is evolving as we review. So it is probably not as transparent from the outside as we'd like it to be.

-With the external scientific community, don't think it happens very often, only at annual meetings. Sometimes there is a public meeting but that hasn't happened much lately.

-We have a higher opinion of our transparency than others do. If you are feeling adversely impacted you think we are anything but transparent. We have had a push to write our documents more clearly with more plain language.

\_\_\_\_\_:  
-Agencies have to be given the opportunity to conduct their own deliberative processes without interferences. Don't

see any one Agency that has yet perfected either pre- or post-decisional information sharing with external public in a way that satisfies anyone. Advisory committees are a nice way to get additional engagement. But the way we set up advisory committees because we are so concerned about perceived bias we often end up recusing anybody with any substantive knowledge of the matter at hand. So what we end of getting engagement from people who may be good scientists but virtually have no expertise in a particular topic.

#### 4b. How satisfied do you feel with the current state?

[REDACTED]:

-Difficult to be transparent to the public when you can't release confidential material. However, the confidential data may help you make a more accurate estimate.

-It is a trade-off: do you want a more realistic exposure estimate that is less transparent, or something that is more transparent and more conservative?

-Within CFSAN: Very FDA-wide: it is difficult to get information from (b) (5) The issue seems to more than a concern over proprietary information; need more inter-center cooperation.

-Unsatisfied. Would like to know more of what is going on in-house and for more information to go out so that people know what we are doing. They have no idea what we do and believe we're doing our job poorly.

[REDACTED]:

-We do only what is necessary, only what is mandated by Congress, the FOIs, the FR publications. We only do the minimum. We can do more, but Risk Manager group of people do not support this opinion.

-If there were more reviewers, more staff we would have more time to be transparent. You could have a designated a group out there to "toot the horn".

[REDACTED]:

Has improved. Allergens were considered a sensitive topic before (all articles had to be approved by [REDACTED]), but now are more open to transparency (just goes through [REDACTED]).

[REDACTED]:

It's hard to get anything out of the Agency and get it through (b) (5) . The (b) (5) are an impediment. They draw a hard line on what is guidance and what you can say in public. That makes it hard to say anything valuable in public without going through the lengthy guidance review process.

#### 4c. What, if anything, needs to be done to improve transparency and engagement? Website

Post some of our memoranda on the web site; GRAS does some of this.

- Website is terrible! People cannot find things.

-Improve web site internally and externally.

-Make the website format a little more user friendly. Maybe via the press office. [REDACTED] has a team working on this.

-Website improvement. Allow this information to be available on the website in an intelligible way and a navigable way. Perhaps we need our own CFSAN website instead of the links from the main FDA website. Provide a list of products being reviewed and not just point them to FR entries. Make it more user friendly.

[REDACTED]:

-We are trying to put all paperwork associated with a food contact notification on the website.

[REDACTED]:

- Internally, there are not many places to go for information on current risk assessments/safety evaluations: Can see how GRAS substances are done on the web-site, but not many others. Could use web-site or e-mail distribution to show the current evaluations that are being worked on as a means of calling out to other experts in the Agency.

#### Interact w/public

-There is major frustration when people have their minds made up. Need to figure out how to get the message out. - How do you show people where to look?

-Scientists don't necessarily have the training to address the public. Need to improve.

-Not so much now, but in the past when a risk assessment was finished, there was a detailed and lengthy discussion about safety and potential controversies. Issues were addressed/explained. But things were held up so long (b) (5) that relevance may have been lost.

-More interaction with the public: editorials and articles to counter accusations from the top.

-Try to present more information in a consumer-friendly format (laymans terms)

-Be more proactive - get the documents out there so people can take a look at them.

-At some level, let them know that we are looking at certain topics and provide information on how these are tested. Instead of going through the media, which got its information from somewhere, not necessarily a valid source, if they could get their information from us it would increase our transparency and also help them understand that we are trying to protect the people.

-They need to continue their outreach efforts. This was part of the National Conversation on Chemical Exposure and Health, get special interest groups together and ask people that want to comment what they want. There is a community outreach group, but I see on the Web like everyone else.

[REDACTED]:

-Can benchmark other agencies and the way they work with the public. -EFSA and NICEATM (U.S. Agency for alternative testing under NIH, collaborate with ICCVAM). Both of these organizations publish their reviews, full reports, identify all panel members, include agreed upon approach as well as dissenting information. We publish in the Federal Register, but many details are not included. It is difficult to follow the logic supporting the decision that was made.

[REDACTED]:

-FDA is trying to make memos available publically (after redaction to remove confidential info). Get information out to consumers to avoid misunderstandings. The source of the information that is out there may be incorrect or the public gets the information in the "wrong way" which results from side-tracking or back-tracking. Need to educate the public via certain program.

-A lot of big news is publicized in the Federal Register, which is not a good forum for the public. Need other means of transmitting to other areas--places where industry and the press will look

-Educational outreach via regulatory and risk assessment course work, seminars, guest speakers, courses.

-Need to hire someone with a Ph.D. in perception. The biggest issue is perception. Maybe we should tell people how many compounds are not approved to show that it is not a rubber stamp program, or have them look at how few have been withdrawn once approved.

-Need to communicate better to correct misunderstandings. Improve web site: not very searchable. Need a search engine that would access info via a key word. In the past FDA has addressed issues of transparency for a specific topic, and the supporting info has been generated, but people can't find the information on the web site.

Communication people are not fully in touch with the work being done. They are too far removed from the work to be clear on the results. Establish communication people within the program so that they fully understand the issue when they put the word out.

- Because of the proprietary nature of the work and the concern that anything said by the Agency may draw significant attention, individual regulators feel that they should be careful not to say anything at all because don't know what type of impact that might have. Need a culture change. If scientists and regulators were encouraged to talk and ask questions, but be aware. Obviously you cannot give away proprietary information. But we are scientists and we should be able to ask scientific questions wherever we are without feeling like we're speaking through this megaphone.

-We need to find a way to get across to the scientific community, the public, and all our stakeholders how the process goes through, what we actually do to do these risk assessments. There is too much concern from the outside especially from the non-government organizations (NGOs) that we are prejudice against industry.

-We are doing okay with engagement, we are making an effort. We have tried newsletters. We have a group within CFSAN that is charged with public communication.

-We need to build confidence in all reviewers to develop public speaking skills. Then you wouldn't just have a select few that do the talking. Anybody could be available to talk.

[REDACTED]:

-It would be good to have a dedicated spokesperson (press person?) for dealing with specific science issues in addressing outside groups, especially for key offices. The Office of Communication may do this.

-Concerns about statements being taken out of context. There is a price to being too transparent.

[REDACTED]:

-Increase the release of scientific assessments and regulatory information and make it more accessible and understandable to outside groups through different mechanisms. The Federal Register (FR) and docket system are too obscure and too difficult for most people to access or understand. Need to release more information through media outlets.

[REDACTED]:

-Try to create fewer response-only situations, which gives the impression they're only speaking up because there's a problem. There should be more free-flowing information, maybe via Twitter, Facebook, or other routes to establish more constant interaction.

-We need to find ways to interact with external community with transparency. It's hard because we are revealing why we are making decisions. FDA is billed as a science-based agency but decision-making is increasingly less reliant on the science and more reliant on non-public health decision factors (economics and politics).

-Interpretation of transparency - mindful to our end audience. Shouldn't force people with specialty training to write their materials in a way it is understandable moderately educated lay persons but they lose the technical punch. Write and FOI in plain language and writing things so that a reasonably well educated reader could understand what you are saying. Determine who the target audience is and pay attention to the audience.

## Scientific Meetings/Publications

-Should send people to meetings who are actually doing the work (vs. the "big name"--you may not get all the details); trade associations ask for the right people, but bigger conferences want big names

Can publish in the literature, but this is tough.

-More publishing in appropriate journals. Get more information/articles to the trade press, but time constraints.

- Need someone to summarize the research being done on hot-button issues. What's out there, what's being done? Newsletter at Center and/or FDA-wide levels. There should be a mandate from above to publish everything that's done in some form. If we're going to use it, and we're going to expect other people to use it, then we should publish. Believes the Agency is too worried about putting information out and getting bad press: "the science is the science", and it is sound. What is the concern over an issue like trans fats?

[REDACTED]:

-Far too little exposure; bigger presence in the scientific community: EPA does some, FDA not enough.

-Publications in journals that are widely read, presentations at scientific meetings (big ones), position papers, and editorials.

- I'd like to see this unofficial "gag order" on FDA scientists [speaking at scientific meetings] replaced with some training in how to ask probing questions that bring out the meat of the matters in such a way as to promote discussion, consideration, growth, and learning for everyone's benefit.

[REDACTED]:  
-As an office at least for food additives, we really don't publish much when it comes to our methodologies and our current projects. That is something we know as an office, but maybe we need to take the time and step back and either put stuff online or publish the basic methodology for exposure estimates, or how we combine EDIs with ADIs. It might be worth pausing and taking a step back instead of jumping into each new project as fast as we can because we are getting a lot of projects in right now.

[REDACTED]:  
-The safety information and a lot of the other information in these submissions are clearly public to anyone who has looked at the question. So it could be segregated.

[REDACTED]:  
-It's crucial for toxicology researchers to get out into the community and publish, present their work, serving on panels, and review other people's manuscripts.

[REDACTED]:  
Has improved: more scientific papers are being published. It is still difficult to get guidance documents out because of potential errors

### More info from top

-Periodic updates--like the Center Management Notes--of what is going on.  
-We should expose more about the steps we take and how we draw our conclusions. Regulations may change, but the science stands; therefore, we should not be so hesitant to put the information out there.  
-More official commentary from the top. Further down, can address the technical issues.  
-Change needs to come from above: need to remove some red tape, or maybe have an office liaison to get things through in a timely manner.

[REDACTED]:  
Sometimes transparency and engagement issues are the responsibility of upper management (Agency) rather than at the Center level. Must have the support of the Agency level because they understand what is secret and not secret.

### Ext. peer review

[REDACTED]:  
External peer review from other government Agencies.

[REDACTED]:  
Might suggest that the National Academy of Science (NAS) approach would be better to look at it. The NAS approach says everyone has a bias we just got to say what it is in the beginning.

### Engage industry

-That is my conviction that I had to convince my leadership, my management, and everyone in my Office that it is a win-win situation for the Agency to have a contact in these industry bodies and to provide a regulatory perspective before these industry bodies make decisions. So with the input from a regulatory angle they can consider these things ahead of time before decisions and actions are taken that fire back on our side. That is much more needed that there is a true active collaboration and participation of regulatory people in how the world is happening and how industry issues are shaping up before they are shaping. None of this can happen unless it is sanctioned by management as a worthwhile activity. Right now it is the exception, not the rule. It should be the rule. Industry usually welcomes us with open arms. We should have regulatory liaisons sitting there that also report back to the Office in an effective manner. So that interaction is giving the Agency a heads up of what's coming or what's happening.

### Internal comm.

[REDACTED]:  
-Internal engagement: has never seen a formal chemical risk assessment that has been distributed or made available to the whole center; no place for it to happen.  
-Group meetings. If issues are to be discussed, it can't be a relay of one person back to who is in charge

- Internal: need to do a better job of sharing in-house what's been decided and why: once a decision has been made, need a discussion. It's not enough to just make the information available.
- Internal: more interaction, collaboration, could be more trusting. External: not needed. Wouldn't provide much, and could get us into trouble.
- Internal: improvement would help to expedite the review process and get more deserving products improved.
- Need more communication across division. Create a database where all the review that are written can be published.
- More information sharing, but not sure of the route because there are too many e-mails already. FDA Notice, CVM News, CVM Office News

## Other

- ████████: Criticized for venues where they share the information, but trying to move toward better exposure  
Need more outreach to scientific community. Presentations at scientific meetings (big ones).
    - Scientific transparency can always be improved. The problem is with the risk management part of the assessment. Risk managers list decisions, provide general discussion. No one requires that they go in-depth on this: how the analysis occurred, pros and cons for each issue, and questions that arose within the group concerning individual issues, and how the questions were resolved.
  - ████████: Improve communication and sharing research. The two labs can complement each other's research rather than compete.
    - They could capitalize more on desire to do well and abilities or connections (e.g., with NTP). Manager needs to be more supportive of employees: help with problems, get protocols through, provide support personnel. If project is relevant to FDA, why is this sort of situation allowed to go on?
  - ████████: Not good at re-evaluating decisions for their impacts after they're made. Should be part of the role of the regulatory agency for future reference. Was it a good decision? Did it accomplish what we wanted to accomplish? Could it have been done better?
    - Get guidances out faster for new technology (e.g., nanotech)

## Expertise/Training:

### 1a. Do CFSAN and CVM have the scope and depth of expertise they need to fulfill their chemical safety regulatory obligations and meet today's (and future) chemical safety challenges?

They always need more people/fresher knowledge

-They hire special skills when they can, but hiring is difficult.

-No; need to increase both

[REDACTED]:

Don't think so. One or two experts are not enough. Now two pathologists, formerly there were 19. Two cannot look at the actual slides/raw data in making their decision, but it appears that they used to do that. Memos from the 70s and 80s were more thorough, filled with content, facts. These types of memos are rare now. In addition, with a large group, you would need to convince 19 people of your decision. Now you need to convince only one, and no one else is an expert in this area--they won't know. There should be proper outside vetting to establish true expertise; publications aren't always enough to confirm someone as an expert.

-We do have an "expert" list for different products. All of these experts are CSOs (i.e., that is their area of interest). Scientifically, an "expert" should have in-depth understanding of both history and emerging aspects of that area.

-Could use more experts. Do an excellent job with what we have, but don't cover all the basis. Try to recruit carefully to off-set retirement. Tough to compete with industry for good chemists, difficult to convince them to come to the government, and the hiring process is not good.

Yes. Strong scientific range of expertise.

-Regulatory reviewers are out of the lab, so collaboration with ORSA is important. They are on the cutting edge. Have been using them more when they see new technology coming out.

-We have a wide expertise but concerned about the new stuff and the future things. What are we going to do about Tox 21data? How will that impact our regulatory processes?

-When saying depth of expertise referring to people that have been here awhile. Everything that has been done here lately is to encouraging people that have been here awhile to leave. Largely we do, but you can't replace someone that has been here a long time. But have heard managers say, "There is nobody here that cannot be replaced." I feel years of experience and "institutional memory" are very hard to replace. People that have requested to work off site have been told they can be replaced. You cannot automatically bring in someone with depth in scientific review.

[REDACTED]:

-Scope of different types of expertise. Good range of different specialists. Could use more depth: the expert on pharmacokinetics is swamped.

-Scope: technical reviewers have good expertise, but don't always know who each other are and are not encouraged to collaborate.

-Toxicology, chemistry, regulatory (consumer safety officers)

- Yes. Different fields are represented. All Ph.Ds. and hiring more.

- We have the amount that is practical, but target issues keep changing, so it is difficult to staff up with enough expertise to cover potential issues.

-We have a lot of depth in certain areas. We have a lot of smart, motivated people. Certainly now because there has been a lot of turnover, we now have a lot of people that are up on the science and have a lot to give. It would certainly help for utilizing that expertise if upper management and management in general recognized that people do have expertise and treat them like subject matter experts (SMEs).

-Think CFSAN has the expertise. A lot of the toxicologists come in with having done research in the latest area of concern or the newest technologies. But these people get frustrated because why is the FDA not involved in this area and why we are not doing more in this area. The expertise is there but we do not utilize it.

-We have a lack of depth of expertise. When one person with an expertise leaves or is missing no one else can step in and help out if there is more work to be done in that particular area. We have this idea about having one expert per specialty area. This might be short-sighted and also gives the wrong impression to staffers, there can only be one person.

[REDACTED]:

CFSAN has both the scope and the needed range of expertise for current regulatory obligations. CFSAN experts are also very competent and able move into or understand new areas as the need arise. Limited numbers of people and time constraints limit the ability to address new challenges appropriately. Complex and challenging new issues (e.g., endocrine disruption, new guidance development) require sufficient time for in depth analysis and building of

expertise.

-Within CFSAN in our particular Division we do. We have a constant influx of new graduates (chemists, toxicologists, and environmental reviewers) that work with us, are hired, and get experience, then they move elsewhere. They bring with them the most modern science that's available and recent expertise in toxicology.

████████:

-████████ could be better served if they had an on-staff veterinary pathologist. FDA is barebones when it comes to in-house toxicologic veterinary pathologists. That is why CFSAN Pathology also does consultation or collaborative work for CVM, CDER, CDRH, and even CTP. The number of toxicologists at █████ is also diminishing due to retirements; more permanent toxicologists would benefit the safety assessment program.

-The problem I see is people get hired for their expertise, and as soon as you are part of this institution, you are not considered an authority to listen to anymore. They hire an expert and then don't want to listen to them. Based on that same attitude the Agency has a tendency to go to external panel review instead of engaging the internal expertise they already have. In order to keep your scientific value as a resource and as a respected member of the scientific community it is absolutely crucial to allow the FDAers to participate in professional meetings, discussions, and issues.

-I don't really know where all our other expertise are and where they are positioned. That would be something that would be very good for everybody to know, there should be some sort of a database that is accessible to everybody where we can find this out with a finger click.

████████:

-In my Office, for Food Additives, the chemists really don't know how to do the exposure estimates and it is expected that they do this. They know how to do them but there has to be more training or more people hired that know how to use statistical programming and work with large databases. Because a lot of the number work can be done in 5 minutes, not 5 months if the right expertise is. It's hard to change a tradition and it's hard to defend why a different skill set needs to be hired in a certain center.

████████:

-We have current expertise is going to retire and will be lost if not back-filled. Many positions are 1-person deep.

-Not sure. Within the group, it seems that they are coming close to achieving the scope and depth they need; however, they have not been able to replace people who leave.

-Need to be judicious in acquiring new staff to expand scope; new staff members need to be able to multi-task

- For research, the scope is limited by chemicals they've been given to study. Depth is weak. Expertise is pieced through the center. The █████ and █████ may both have the expertise, but do not talk to one another. Enhance expertise provide line of communication between the groups.

-Research is one-person deep in expertise and need to build for future. Scope could be improved by setting up an integrated product team - █████ (toxicology) and an integrated chemical safety team - █████ (research staff might facilitate). Example: arsenic – utilize depth of expertise use and integrated team. Scope needs to be expanded.

-Never have resources you want. Gets back to an enlightened management which allows flexibility. Before they were pigeon-holed into a narrow area but now the management is more broadly focused. Priorities can change quickly. i.e., Adapted quickly and responded to the Gulf oil spill.

████████:

-For exposure, no, need more people. They have lost a lot of expertise that has not been filled. Need to assess what we have and what is missing. They are doing this and trying to plan for the future.

Need more people, more knowledgeable supervisors. Before, the program was led by scientists; now it is led by lawyers who don't know science. Need more scientists at the higher levels to help evaluate final decisions. Feels that scientists are not as much appreciated as they were before.

-Without an inventory, how would you know? Hiring tends to be uncoordinated and rarely looks at the specialty needs of either the group or the program as a whole.

-There is definitely a depth problem, we have few people and we all have to be general toxicologists. Forget about redundancy in expertise, we are lucky to have one expert.

-One of the main issues in terms of our toxicologists is that many people have retired and have replaced hardly anyone. We have lost a lot of expertise and years of experience.

████████:

No. Always need more for the future, but can't staff up in advance. The existing level of expertise is impressive. Also, how can it be applied to new situations while maintaining the level of work? Can't have "extras".

-Yes. Good scope and depth. Have been hiring more staff with research background, recent graduates who are

more familiar with state of the art techniques and have access to peers in the field.

-Definitely. We have a wide variety of expertise in different technical areas. Can also seek external help: can go to CFSAN for pathology issues. They are always willing to assist us.

-Yes, within <sup>(b) (6)</sup> group. They have experienced and tenured people. Have history on established drugs. For the future, they need to bring in good people to establish a good foundation for when new things come in.

## 1b. In what areas do we have greatest expertise?

Strong chemistry backgrounds.

Chemistry and toxicology

Organic and polymer chemistry

Molecular biology

Neuroscientists and traditional toxicologists.

████████:

-Lacking industrial expertise and field experience (especially for consumer safety officers), but otherwise they have a good range of expertise: "world class in regulatory chemistry". Balance scientific strictness with the needs of regulatory safety.

Exposure assessment for food additives/food ingredients/food packaging. Also in developing specifications for food additives. Working with Codex on compendium of specifications for purity

-We have good expertise in human intake exposure evaluations, good experts in reproductive toxicity, carcinogenicity.

████████:

Broad expertise-not weighted towards one area or another. Do a good job of keeping a well-rounded division.

-Have encouraged development of areas where there is a lack. Well balanced.

-Senior supervisors in chemistry and toxicology know regulatory toxicology and work hard to be consistent.

-Carcinogenicity risk assessment, general toxicology risk assessment, reproductive and developmental toxicology

-Consumer safety officers: wide area of expertise (chemistry, toxicology, nutrition)

-Exposure assessment. Toxicology is good, but it is more complex, and thus more difficult to maintain expertise.

-Whole animal toxicology, carcinogenicity, genetic toxicology, QSAR, *in silico* (computer modeling for toxicology)

-Gene tox, reproductive tox and developmental toxicity. Have some depth in immunotoxicology (b) (6)

████████. There are some neurotox people and some heavy metal experts that are good.

-We are good in *in vivo* toxicology, *in vitro* toxicology, genetic toxicology, carcinogenicity *in vivo* studies

████████:

Toxicology, Chemistry, and Consumer Safety Officers

████████:

Food Additive Reviews and Food Packaging Material Reviews

████████:

Our greatest expertise seems to be in Chemical analysis and Regulatory Writing.

████████:

Dermal toxicology, nanotechnology expertise (6 people), reproductive toxicology.

-Within █████ have people with 40 years of experience; have started to back-fill

-Old technologies: animal feeding studies, but missing translational capabilities for these studies, especially in reproductive areas. Toxin work (closed down now). Chemistry, but some very specialized (lipids, foods) individuals. Immunology (animal modeling, genetic backgrounds, risk assessments with translational component).

-Trending more to being generalists. Before we were the premier laboratory in genetic toxicology, but not sure there is any area of toxicology we are regarded in that same light. From interviewee's perspective that is not a bad thing.

-Greatest expertise in microbiology and molecular biology

-Reproductive and Developmental Toxicology Program, we have a strong Nanotoxicology Program, a strong *In Vitro* Toxicology Program

-Immunology, classic reproductive toxicology, endocrinology.

████████:

Modeling in dietary exposure. Good mix of technology and understanding the scope of the science.

-My impression is that neurotoxicology has been a very popular specialty in recent years and so we have hired many neurotoxicologists in spite of the fact that this is not necessarily the predominant organ for food toxicity.

-We are in a transition now, 6 months ago I would have said there is great expertise, but a lot of things have changed. We have good expertise on contaminant safety hazard assessment and trace elements

████████:

Well rounded in toxicology, chemistry, food technology. Mostly good on medical background.

████████:

Small chemical entity food safety.

Aquaculture; drugs in fish

Toxicology, microbial, residue chemistry, biostatistics, environmental

-Well-rounded team: animal science, chemistry, physiology. They have filled in to cover expertise

-Human food safety

-We have outstanding well-rounded toxicologists in classical areas, but we fall off in specialized areas.

-Residue chemists, good toxicologists, great analytical chemists (work done by contract laboratories), animal scientists

-We have very good people working on risk assessment. We have good knowledge of endocrine disruptors, we have *in vitro* and *in vivo* knowledge, we have people with good training in molecular toxicology, reproductive toxicology, developmental toxicology, and general toxicology, and some expertise in neurotoxicology.

-Expertise in regulating veterinary drugs, both in the review aspect and the research aspect

-Animal feeding, animal physiology

## 1c. Where do we most need to increase our scope and depth of expertise to improve our programs?

[REDACTED]: Could use more food scientists rather than just people with chemistry backgrounds who learn what they need to on the job.

-More people across the board. Need to determine the focus. If they are going to add more to our mandate (e.g., post-market), then need more people.

-Put more chemists on staff, including an industrial chemist.

-Need more “bodies”. Could use more people with actual risk assessment experience to be available/work at the mid-level and give suggestions.

-Shortfall in microbiologists in her office; rely on those in office of food safety. Expertise needed for produce. Can leverage with EPA.

-Nanotechnology: this changes with the current hot topic.

-Go back to the toxicology side of things - handling the new tests that are developing in a regulatory environment that are not the standard. Are they meaningful to us?

-In particular feel that junior employees should be trained to replace senior employees (when not in office, changes positions, or retires) so that we have a continuous experts in all areas.

[REDACTED]: Mathematics and statistics. Can get this from other offices but not within the division

-Immunotoxicology-especially developmental toxicity/immunologist.

-No specialist for endocrine disruptors, although some overlap from in-house staff (developmental, neurotox, etc.).

-We have no dedicated in-house statisticians, few senior people with up-to-date knowledge of food packaging toxicology, and no biological systems modelers that can help us move from the “count the dead rats” paradigm into the arena of 21<sup>st</sup> Century Tox, high-throughput testing, and pathway-based toxicology. Many of us newer folks have the right backgrounds to understand and utilize such info but we need better access to those who can actually help guide day-to-day Tox reviews.

- While there is always a need for more expertise in the complex interdisciplinary area of risk/safety assessment and all the related disciplines, the real need is to integrate the expertise that we have by recognizing the profound interdisciplinary nature of this activity. Such recognition would galvanize the need for mutual team efforts to solve difficult scientific and policy issues.

-Need new blood in “omics” and in vitro testing; however, just a few. Neurotoxicology, pharmacokinetics, and metabolism, staff for tracking/responding to emerging trends (via recruiting efforts and training)

-Changes with the need of the moment. General toxicologists may cover a broad range of specialties. Needed reproductive people for BPA.

- Need better access to scientists with expertise. Roster of scientists willing to serve as short-term consultants or advisors.

-More training or expertise in how to use these new high-throughput *in vitro* methods to incorporate them into reviews as they become more and more available and prevalent.

-Pharmacology background or pharmacokinetic modeling background and also someone with more of a background in metabolism

-Now with the increasing emphasis in reducing animal use in safety assessment (high throughput technologies, TOX 21), think we will need to increase emphasis on training personnel in these areas. We need to train more personnel in toxicogenomics and get a better understanding of epigenetic mechanisms of carcinogenesis. Training is essential; we need to be very proactive on this. We cannot just wait for the technologies to mature and say it's not going to make it.

-Think we need more toxicologists especially in CFSAN - [REDACTED].

-Endocrine disruption and pharmacokinetic modeling.

[REDACTED] ( [REDACTED]):

Increase exposure data and risk assessment.

[REDACTED]: Toxicology has been the stepchild of the Center for a long time. Since I have been here toxicology has atrophied badly. This is not good thing in the wake of Tox21. If you run all these *in vitro* assays and you don't have a good toxicological understanding of *in vivo* issues and translation to man, the interpretation of these assays is bound to be wrong. As an Agency we need to revitalize toxicology. We used to be the Nation's and global leader in toxicologic assessments as the FDA regulating drugs and foods. We have slowly but surely lost that reputation. The entire tox

concept at FDA needs to be revised, revised, and revitalized.

■: -Was hired full time to help with the mathematics, statistics, and programming that is needed both to do the calculations we need and to understand when people come to us with data, what they did and to be able to translate it in a sense. There isn't really anyone else in the Office with an engineering or mathematical background. The chemists are very smart with what they do, but they don't have that mathematical expertise and are expected to do that piece. It would be optimal if they had more people with mathematical backgrounds. It's hard because they can't just hire anyone. For the Office it says to hire chemists for chemistry reviews, even though there is more than just the chemistry piece that goes into a safety assessment, chemistry-wise.

■: -There are two pieces and it is the math side that we need to bring in. EPA has that. They have two totally different divisions. They have the chemists and the math and they pair up to do the safety assessments. Right now we only have the chemists that do everything. We need to pattern it after the EPA structure.

■: -Understanding, developing, and using models or systems that are not the traditional ones that toxicologists use. How to detect and deal with potential emerging issues.

■: -Knowledge of modern biochemistry, biotechnology, mathematical analysis (of data), pharmacology, physiology and **modern** toxicology are fragmented, with no Office / Center support for significant improvement of individual or Office expertise

■: There is a big gap in age and expertise. There are people with 30+ years of experience who are leaving/have left and cannot be replaced or back-filled. We don't have mid-career people in our branch.

Labs are lacking depth in reproductive toxicology (one), in vitro screening,

-Need skilled technicians who are actual skilled technicians, not animal care personnel.

-The level of expertise needed for this job has changed.

-Need ability to convert ORISE fellows; when their fellowship is up, they're gone, and their training expertise is lost.

-Need plan for covering critical areas.

-Can also consider contract work, but need a well-designed protocol prepared by inter-disciplinary team and upper management decision.

-Nano expertise. The group needs to be versatile; however, there is the potential for a "jack of all trades" situation to develop.

-Ability to address emerging issues: Genetic, molecular, and chemical capabilities are needed; not many scientists are able to integrate this type of information. Need seasoned individuals to assist new hires. Proteinomics, no array technology Need to bring up to 21<sup>st</sup> century: individuals who are able to make judgments and do integrated, complex analyses.

Improve communication between groups. Set up more of a team approach to Chemical Safety Evaluations; get people from ■, research, other offices. Using an integrated team approach might facilitate a better assessment from the beginning. Cross-populate expertise; scope is limited by keeping it to a particular branch/team/office.

-Nanotechnology

-We need to get more depth across the board with everything we have. Including even our strong points such as repro tox. If we lose one person the program starts to fall apart; we need more depth.

We also need to build up on our people with *in vivo* expertise and molecular biology expertise.

-GI, a person who really knows gut from the point of view of pathogenicity of microbes as well as the immunology and gut hormones; renal toxicologists; physiologists (well-rounded, not people that just graduated); neurotoxicologists (endocrine, immune, and neuro); inflammation

■:

-Retiring toxicologists rehired as a part-time. Overlap time to train new employees in the process.

■:

-Reproductive toxicology is unpopular among students and we probably have few experts in that field.

-We need reproductive toxicologist, cancer biology toxicologist, and renal toxicologist.

■:

Pharmacology, pharmacokinetics/dynamics for dealing with drug residues.

-CFSAN should get more involved in antimicrobial resistance; ■ has the lead on this (resistant bacteria in animals)

-Developmental biologists, more medical officers (neurologist), oncology.

- [REDACTED] could collaborate with other offices on chemical safety assessments.

[REDACTED]: Because of TOX 21 we are going the molecular basis. People will need to be trained *in vitro* methods.

[REDACTED]: - Proprietary issues are a problem, but can be worked around. They are working to set up confidentiality agreements with Canada (VMA, VDV, CFIA and others) so that we can share data: quarterly meetings, RCC program to coordinate with Canada on vet drugs.

Could leverage what we have better with more information on what's available. Need to bring in those with expertise with large molecules. Increase molecular biology expertise to address systems tools. Could increase expertise in stem cells, genetically engineered animals, use and interpretation of structure/activity, interaction between *in vitro* and *in vivo* models (Tox 21) to create practical regulatory tools.

-Pathology: have to go outside the Center, but there is not always a need for this.

-Ability for scientific/technical writing. Everyone has different training coming in. Some scientists (e.g., vets) have never written scientifically.

-In residue chemistry, we could do a better job on how we're handling the analytical methods. It's a big issue because the sponsors have to develop a method, but it might not be the method that USDA or CFSAN want to use for their compliance program.

-But things like hormones (endocrine disruptors), nanotechnology, carcinogens, and biotechnology; we need narrow expertise.

-Need more toxicologists but resources don't allow it: someone that knows about all the new stuff that's going on, the new analytical methods.

-What we need to do is think about more of a matrix approach. So if there is someone across the street with a specific expertise that we don't have then we need to be able to use that expertise. We need to integrate. It needs to be better coordinated. Expertise should be shared across the Agency. We have to get out of the line management only (stovepipe) mentality. The way we are set up now does not permit this.

-We need more risk assessors who aren't expert quantitative modelers, but actually know how to talk a toxicologist or scientist through a risk assessment paradigm for the first time. We need to have some bridge between the analytical quantitative risk assessors and people that are actually doing safety assessments and risk-based assessment and weight of the evidence assessment; great if we could do more pharmacokinetic modeling for safety risk assessment to understand absorption

-We need more administrative people. Don't distract scientists with paper management. Would be nice to have an editor for some of our documents. Codex has a professional editor.

[REDACTED]:

-We need to be "less do it by the regs" and be more risk-based on our approaches.

-We need more risk assessors. We need more risk assessment developers, We need PDK people. We need people that are experts in interspecies extrapolation. We need more systems biologists, people that can tie things together and tell the story better. We need more molecular biologists co-trained in physiology. We need more people to integrate things as opposed to specific subject matter experts; think risk assessors can perform that function.

-Cross training

## 2a. Can CFSA/CVM get adequate external expertise when needed?

[REDACTED]:

- Yes, but tough to get going, such as Food Advisory Panels
- Depends. Contract stuff: yes (when money is available). Industry is tougher when it comes to additional information.
- Not sure. Believes she is not encouraged to go externally for expertise at her level.
- Sometimes yes, but usually if “calling in a favor.” For premarket review it is difficult due to confidentiality issues.

[REDACTED]:

-Yes. The problem is how it will be perceived by the general public. The concern is conflict of interest: did we pay that person to do the study. Plenty of people with expertise, but how will they be perceived “We need to hire somebody who has a degree in perception.”

-Yes superficially, but practically it is difficult, because the rewards aren’t there for the sacrifices that the outside experts need to make.

Was told that “we don’t do that.”

[REDACTED]:

-We can always convene a scientific review board. It works well and is not too hard for the Agency.

[REDACTED]:

-No. The process is cumbersome and time consuming. No structure for grants, contractors: tough to get grants through. Need to evolve to where we can do it at the Center level.

-Yes. Not often, but as needed. In a recent case were able to contract specific external expertise.

-Collaboration can be done on a personal level. If you know somebody, pick up the phone. This is much easier.

[REDACTED]:

-[REDACTED] had a practice of asking for help from CDER Pharm/Tox reviewers for special cases that was used rarely but effectively. Not sure if other Offices do that. My experience was that [REDACTED] Division Directors and [REDACTED] staff were happy to help out.

[REDACTED]:

Yes. Can use prior connections; informal. Within government can be helpful.

-Consulting services take time to obtain when you need answers right now.

-Difficult to get neutral help outside of the government.

-Food Advisory Committees are difficult to assemble. Need an easier way to do this.

-Should be able to invite scientists here and pay for them; streamline the process for getting expert opinion.

[REDACTED]:

-Difficult: There are limits. The clearance and weeding process makes the experts you want unavailable: Academia can have COI with industry, so we can contact them, but are limited. With other agencies, the difficulty is identifying contacts.

-Integrating the academic response (even within other Agencies) to the regulatory environment can be a problem.

- Not attempted.

-Yes and no. Can e-mail questions to individuals, but it is difficult to get speakers in.

-Yes. E.g., we go to CDER for help with cardiovascular

## 2b. Why or why not?

No method for finding an expert when you need help with something.

████████:

The formal process for getting clearances for this is burdensome. Difficult to identify the expert/organization that you need. Confidentiality issues

████████:

-There is no reason why we cannot get any special expertise we want within government. It is a matter of process and making it happen. There is so much expertise within the government scientific agencies, themselves, and they seem eager to help us. But we need to ask, and not cower behind some insecurity complex that makes us reluctant to ask for help.

-Need to figure out how to change this. We rule out industry because of COI, but the EU does use industry. We could use them but not let them vote.

-There is not a clear SOP or mechanism in place to seek external expertise out.

████████:

Tough to get past COI criteria; academia out because professors get money from companies.

████████:

It is difficult to get permission to discuss sensitive policy issues.

████████:

-We don't work hard enough to obtain this, probably because we don't feel it is necessary.

-W Budgetary constraints. People respect █████ and are willing to come in/provide support. Can get general.

-Specific help: Usually we are dealing with proprietary compounds, so difficult to get.

Difficult to identify who and where to look for the expertise. A database would be useful. CFSAN lists people with different language skills. █████ lists expert reviewers (14 and 15). Traction might be useful. People can put their resume there, but people aren't going to search that. A database would be better.

-Constrained by proprietary information. There needs to be a formal process.

-There is no criteria when doing a review that you need to get external expertise. It's not that we can't get it but is all the procedures (confidential agreements) associated with it, all the administrative things. Also, to get the right person within that limited time to address the issue is difficult. So you see people making decisions they think they know just to make the decision because they are assigned a certain work.

-It is difficult is picking up the phone and talking to 2 or 3 experts and be able to tell them enough to get input in a useful way. There are a lot of understandable but very difficult restrictions placed on our ability to do that.

### 3. To what extent should we focus on acquiring general as opposed to specialized toxicology expertise?

■: If we have a competent general scientist who can identify an issue and go to an outside expert for help, then generalized is enough. If not, then we need specialists.

A combination is best: Broad education with some focus in an area in which we are interested. Sometimes there isn't time to get the needed expertise, or a lot of the expertise that is desired. Sometimes the right person can't get through the system.

-Within chemistry, we have enough general expertise. Need to expand: a nanotech expert or endocrine chemistry expert, or expert in QSAR or computation chemistry. Another thought would be to send staff to risk assessment training.

-If someone is overly specialized, then it's hard to adapt to general work. Reviews cover all different types of food uses. Sometimes as specialists, we need to learn the fundamentals to do the reviews.

■:

-Everyone is expected to be a generalist. Need to hire specialists that can be generalists.

-Should focus more on training internal staff; allow scientists to expand expertise within the center to include additional areas.

-We first need to focus on getting toxicologists at all, regardless of whether they are generalized or specialized.

-True "toxicologists" are rare because true toxicology programs are rare. Most have done research on cells vs. whole animals. If we can't hire a toxicologist, can hire someone with good pharmacology, biology, biochemistry background and then bridge the gap.

-General toxicology expertise is seasoned and is gained from people working in interdisciplinary environments that foster such seasoning. These people are scarce. We need to develop them ourselves, not think we can steal the few of them from somewhere else. They can be specialized when they come in.

- Need specialized to address emerging trends. But young people are more molecular, "omics", in vitro toxicologists; they need to be trained here in whole animal toxicology. Universities should bring regulatory people in to discuss their needs. We can interface at the meeting.

- Maintain balance based on what is needed.

-Better mechanism to promote inexperienced staff based on their being good generalists, rather than just on their specific areas of expertise. Need people who can ask good questions.

-Over years specific expertise erodes to become good generalists.

-We should focus on specialized toxicology. Having groups that are comprised of scientists with different specialties is an advantage. Anybody that has specialized toxicology expertise will have general before that.

■:

-A generalist toxicologist approach would be very good. We should focus on that to a large extent as interpretation of toxicologic signals will be a big part of the future and it would be good to do it with an integrated approach rather than a limited, specialized approach that focuses on either gene tox or microbial whatever.

■:

Tough call: DABTs have a lot of expertise in different areas, but can't necessarily do a specific study type.

-How do you decide whether reproductive or liver toxicology is a greater priority?

-Need to reassess the contributions of a given area to decide whether there is still a need for that area.

-Emphasis should be more on generalized expertise: need to be ready when different issues come up. A Diplomat of Toxicology can be very useful to the program. With a broad background, they can get the rest of the group involved; therefore, a more diverse knowledge base can be applied.

- Acquire general; specialized may not be used to the best of their abilities.

- For research, thinking more of generalized because never sure what is coming. More generally trained could design studies as needed, and gaps could be filled with specialized expertise (e.g., ORIZE fellow). -If too many specialists are hired for a specific project, they might not be needed in a couple of years.

-We need to specialize because science is evolving. Have a general base.

-Now we need to focus on specialized toxicology to address emerging issues and to remain state of the art.

■:

-General: a general toxicologist will develop specific expertise on the job.

-We all BECOME general toxicologists but there is no substitute for having SMEs.

-With respect to chemical contaminants, having general toxicologists is good because you have to do so many chemicals. They all have different effects and so you have to be a generalist and specialize when you have to. The

carcinogenic experts have retired and that's a very specific field. So carcinogenesis is one area we do need specialized expertise.

[REDACTED]: Specialized because they have studied a given area more in-depth can save time; they know where to find information. Best to have a group of specialized toxicologists within an office.

[REDACTED]: -Both. For chemical safety/risk assessment, you would want people with general knowledge with specialization in one certain area because we are not doing just one type of study. Specialization is OK if there is work in a certain area and you don't need to go outside for expert opinions.

-It needs to be balanced. If we don't have good general toxicologists we are going nowhere because most chemicals we analyze have some recognizable toxicity in a range that we look at. Then we hit issues like bisphenol A and immunological issues that most toxicologist don't have a great deal of depth in. So it needs to be balanced.

-Always thought that a lot of this expertise could come from the research side. So when we need the real specialized expertise rather than hire a specialized review toxicologist we could hire somebody to be involved in a research program but who we could pull in and train to do regulatory review on an occasional basis

**4a. Are the staff and resources currently devoted to chemical safety reasonably deployed and efficiently used across the Foods and Veterinary Medicine Program?**

-For Foods, yes

[REDACTED]:

Don't know. Within his division yes, and within the office doing as well as possible. Within the Center, regulatory issues are being addressed properly, but not sure beyond that.

-For what we have work-wise, probably so. With the shift to more post-market review, need to change. The reviews are time-consuming: need to look at and vet a lot of data. Takes time, even working with a group.

-The Foods Program is short staffed. It's reasonable yes but in a relative sense. We are deployed efficiently.

[REDACTED]:

No. The chemical safety programs are very inefficient because they are antiquated. They suppose that individual scientists can fathom the full scientific/policy view for any situation.

-In general, yes. The balance fluctuates, so may not always be right.

4b. It has improved (e.g., post-market initiatives like Na reduction). Additional funds have been provided to recruit temporary assistance; get working resources without long-term commitment.

- The problem is the division between "moving freight" and taking on special projects. Special projects get noticed; moving freight, only if it is not done. Most staff working at capacity; however, a small number do not, and this is demoralizing. Tough to find the balance between staff who are more expert in a limited field and those with broader experience. Limited expertise can be more efficient, but lose the breadth and scope needed to resolve more challenging situations.

-Previously there was a "pool approach" for toxicology, chemistry, and the chemical safety officers (CSOs) where everyone was essentially in the same group and you received assignment across product areas. Assignments were made across the board lending to a wide area of training. Following the reorganization, the scientists (chemists, toxicologists, and CSOs) were divided up by product area (Food Petition, Food Contact Notification, and GRAS). This has been a mistake because now everyone is a specialist in one product area. Everyone should know how to do all types of reviews.

[REDACTED]:

-It is efficient, but issues arise in being able to devote adequate time and people to addressing emerging areas of science or to address an issue in a reasonable amount of time.

[REDACTED]:

-Letting people know who is out there, a smaller directory by specialty. Maybe an Office of Foods Directory of toxicologists, veterinarians, pathologists, chemists, biostatisticians, etc. that could be available to serve on CACs or provide consultations on a specialized or controversial issue for that Center or Office. Most of the people I have met in [REDACTED] and [REDACTED] have been through mutual acquaintances, repeat consult customers, or professional societies such as STP or AGT (Association of Government Toxicologists).

[REDACTED]:

-Yes, in the sense that most of the effort is devoted to the evaluation of regulatory submission and is perceived externally as an important role for us. To the extent that there is any flexibility in the deployment and use that needs change, then the answer would be no.

[REDACTED]:

Getting better. The lab has better resources now as a result of certain toxicology issues.

-Not sure how or the basis for deployment. Some groups can get some resources; some get nothing, but no reason is provided. Personnel may be re-assigned with no discussion.

-Across the foods program better integrated within [REDACTED]. At CFSAN, everyone is sitting in own lane (stove pipe): Research lane, [REDACTED] lane, Chemical Assessment lane. Need to cross lanes

Efficiency is lost where specialized expertise is not used (e.g., brain focus specialist)

-Expertise is not utilized or appreciated properly. There had been incidences when the Center made decisions without consulting laboratory scientists that probably had an expertise that might have affected the final decision that was made. Previously the research and regulatory scientists were joined and this fell by the wayside in the 1990s and has never recovered after the split. Not the best utilization of in-house expertise. Being prepared to move resources where and as they are needed, build that flexibility.

-Under the current budget situation, trying to maximize resources they have.

-No. Nobody knows what individual expertise are. They don't know the depth of their knowledge or lack of it.

[REDACTED]:

-There is a value to stove-piping because experts are working with experts to critique each other's work. Although the trend is toward integrating teams, there was value to the old set-up. Ideally, you'd be able to go back and forth between both set-ups. There is no perfect mix.

-Yes in general. With the establishment of the Office of Foods, there is an increased level of bureaucracy. Have to get everything through a different level. Resources in the trenches are allocated quite well.

[REDACTED]:

-Not recently. We receive numerous FOI requests; therefore, we find ourselves pulling information for these requests--copying/scanning--rather than working on reviews. Doesn't take much scientific expertise. We are not doing what we were hired to do, but it still has to be done.

[REDACTED]:

-We are way too top heavy. We need to stop building programs and start doing work.

#### **4b. What ideas do you have for improving the allocation of staff and resources?**

Currently, there is a strict division by work product vs. area of expertise (tox, chem, and CSO in each division); before, they were divided by discipline, and this allowed them to spread the work around by chemist. Something like this could work again.

-Maybe more unofficial details or requiring details in other divisions.

████████:

-Certain people are under-utilized. May need to shift/re-prioritize workloads; work with division director. When you do good work, you get more work.

-We could use more people but it has to be the right people. When we had the direct hire, we got a lot of people that have not stayed and don't think we were allowed to back fill those positions.

-Shadow, cross training to help out in times of need. Like internal details.

████████:

Some sort of handbook ("white pages") of who is the expert for their area and are they amendable to questions.

-Formal/official consults take time, but would be quicker to contact someone specifically for a small question.

-A way to go to academia with questions without concerns about tipping off the press, asking questions in a public forum.

-████████: They have a diverse background. If resources are not available for think-tank type projects, could do in-depth projects, lit. review. Put 3-4 ORISE fellows on the project, senior people could then QC. Allow people who are interested to serve as well.

-The scientific community has understood for some time that research and understanding in the biomedical sciences needs to be a collaborative enterprise because it is too complex for individuals. Until we understand this, we will continue to perform assessment in the comfortable manner of 50 years ago.

--For the small number of staff who are not working at capacity, some means to oblige them do more. For expertise vs. breadth, consider staff rotation to address this issue. Address issue of reacting to issues that have already been resolved simply because someone important raises the same question again.

-In terms of chemical safety assessment we have one office that does both pre-market and post-market issues when they come up. We are Congressionally mandated to do pre-market on a strict timeframe. It is very difficult to also do the post-market issues when they come up. So either having a dedicated staff to post-market issues or increasing staff so that there is time to handle both.

-For personal career development should allow or encourage temporary details or rotations to gain broader knowledge and point of view.

-Having a bias for ██████████, need to separate pre-market staffers from the post-market staffers. Have designate individual for both but they should be cross-trained in both in case there is a fluctuation of work.

████████:

-Create a system like EPA's ORD with the formation of ad hoc specialty groups that have support to dedicate time to address an issue in a reasonable or expedited amount of time.

████████:

-People need motivation rather than deployment. It doesn't matter if you put somebody somewhere. If you can't get them motivated to do something because they want to do it nothing will get done. Since 2004, motivation has decreased to the zero point. People have given up and don't care. Motivation - change the Center's cultural leadership. The new leadership should focus on motivating the staff to a common goal and to the specifics of the outcome they want to be seen.

████████:

-Math exposure team just like EPA.

████████:

-Somebody needs to figure out a way [mechanism] to be flexible in using resources at same time enhancing the career opportunities for the people involved.

████████:

-Rotations or details should be mandatory for first few years for scientific staff so they learn the full scope of activities. It's going to raise awareness everywhere if there is more exchange of information exchange. People have to move and can't just stay in their little box.

████████:

-Within the division: Form a strike team. The team would change with the next high priority need, when a new strike force team would be formed.

-Communication. If you know the expertise that is needed, you can build the teams needed, rather than hire individual expertise.

-Better integration with CVM to leverage staff and resources; more efficient. Break cultural and historical barriers to get it done. Develop an integrated process. Open doors to the assessment so that it is more transparent.

-We need to bring in specialized toxicologists; some with more *in vivo* experience. We need to increase the depth of what we do have. We need to move into areas for endocrine disruptors and addressing Tox 21.

-We have to know what the needs are. So if we know what type of adverse events are related to a compound, the resources could be allocated.

-Should have group meetings where issues are put on the table and hashed out.

[REDACTED]:

Start with a survey of skills and expertise. Use staff fellow and Commissioner's fellow slots to acquire missing expertise.

[REDACTED]:

-Harmonization with CFSAN's toxicologists would be good so that we can better utilize resources, depending on level of work in each Center. Could shift around if needed. The regulations are different, but the approaches could be harmonized and expertise leveraged across the Centers.

- Could bring in contractors for FOI requests and leave the scientists to do their jobs. The expense would balance out.

-Meaningful cross training is a great idea. Once you have a fully trained and educated risk assessor, toxicologist, exposure assessor, pharmacologist have them trade jobs with someone at CFSAN for 6 months to a year to learn people and practices that they might want to bring back to their parent Center. Then if there is a true emergency and they need help these people could seamlessly enter because they have done something like that. That could go either way.

-Every time you have a fillable position you need to do an assessment for where that position is needed. We have to get away from the mind set of I lost a person I get to hire a person.

-First we need to define scope and needs for the next 5 years. That is difficult because our budget is from year to year. Look at the overview, emerging issues, basic objective, overall goal, and then analyze what we have and what are our deficiencies (part of what these interviews are doing). From there, defining what we need to do then allocation of resources (shifting or maintaining) for these programs or new programs.

[REDACTED]:

-Get rid of silos and start working on a matrix-managed approach. We've got lots of resources scattered all over the place but we don't know where they are. We don't always bring the best people to bear because something has to go through a particular administrative route that limits the extent to which you can pull people in. We need to understand that these are Agency resources, not Branch or Division resources. Expertise needs to be deployed to serve the public not to meet an administrative quota.

### 5a. Are our training needs being met and if not what training types/topics would be most beneficial to the programs?

Need to have more opportunities for outside courses (analytical methods). More hands-on experience with techniques; keep up-to-date

Need to attend more meetings and conferences (now 1/yr, if presenting), at least in town.

-Hands-on workshops with some of the emerging technologies (in vitro tests, nanotech).

-Collaborative efforts with the lab in AL to evaluate things like high throughput techniques. They could help assess if the techniques would be helpful or not.

Having a DABT is a benefit, but all of the training/prep needs to be done on your own. If prep courses were available, maybe people would be more willing to do that. The courses would benefit everyone. Would keep the Agency up-to-date with different areas. Would not need to be specific, but could give an overview of topics like immunotoxicity.

-General toxicology (pathology) courses would be good.

-Better allocation of funds: e.g., [REDACTED] courses in summer, at end of fiscal year, so there is no money left to attend and/or they're already full.

[REDACTED]:

There is opportunity, but budget constraints. New exposure assessment technologies training is available; using more of raw data. Developed seminars with ORSA for new techniques and analytical methodology. Series on different ways of risk management and exposure assessment. Need to look more at what we can do internally

-We need more information on food processing practices and keeping up to date.

[REDACTED]:

-Yes. But mostly by people within the Agency looking for opportunities outside.

-There is a recurring problem with providing training in the form of attending Fall meetings when the budget takes so long to get finalized and no one is willing to pay for them in July or Aug; possibly, longer range development plans could incorporate odd-year big trainings with in-between smaller ones.

--Advanced trainings such as PBPK (Physiologically Based Pharmacokinetic) modeling, systems biology modeling, DABT etc. should be provided, even though these might be expensive and lengthy.

-As a cost-savings measure, some recognition/encouragement of people paying for their own professional society memberships can save meeting registration costs. I think that there is a process in place in the Executive Branch where there are incentives for saving the government money) but it needs to be communicated while not obligating the office to send someone to the meeting necessarily.

-In our office there is no training on how to do the job. We don't generally share our personal search techniques or any details of how we do the daily work. There is not much in the way of SOPs, a manual for new hires, or anything. It is like the attitude is "You have a Ph.D. and should be able to figure it out."

-Exposure to outside information. Allow people to present their work outside and go to meetings. Get training on how a company does production: go through GMPs, HACCP. Need to have practical exposure, a "field link"

--Need to have mentors for new people coming in with respect to regulatory procedures, and these do not necessarily have to be supervisors.

-More opportunities via webinars, online classes. More specialized toxicology courses (neuro, developmental tox). Would help in evolution with animal studies. Cross-training with chemists on how they determine exposure.

-No, our training needs are not being met. Could benefit from annual training (like doctors go through), refresher courses, updates on hot topics in toxicology.

-Our pathology group organized 8 or 9 lectures in the areas of pathology which toxicologists need to understand. And there have been other efforts, classes in immunology that have been organized by groups within [REDACTED], our GRAS Review Group set up an immunology class. But there should be a program here that focuses specifically on new issues that may be coming up, like epigenetics, genomics, and toxic genomics. A co-worker organized a series of three lectures on genetic epidemiology that were pretty well attended. But these have been individual initiatives. Having a group that might recommend courses to be taught and help organize them. It might be an ad hoc group that met once a week or month to look at what we could do, what areas need to be addressed, what was coming over the horizon in terms of toxicology and the science itself.

-Toxicologist continually need to be trained in basic toxicology, also continual training in the Good Laboratory Practices and Good Clinical Practices. It is up to the individual toxicologist to maintain that training, but there should be a minimal retraining period for everybody.

-Absorption Distribution Metabolism Excretion (ADME) or the short way of say this is PK (pharmacokinetics)

profiling. Also, physiological based pharmacokinetic (PBPK) profiling.

████████: -Our training needs are not being met because training is tied to travel. Travel is so limited and so training is limited too.

████████: -Some type of training is needed on: an introduction to databases; statistical software; and more communications training

████████: -Would like to see an active program that allows people to go out to details or sabbaticals or some experiences in academics or other Agencies. Get experience from the outside, not just going to classes or seminars. Something equivalent to what happens in an academic environment.

████████: -Educate us on the whole program first. She knows only what she is involved in. She knows the scope of what FDA regulates, but not the specifics of what and how it's done in different groups and offices.

-CFSAN ran an in-house toxicologic pathology course a few years back. The toxicologists who attended should be asked whether the training was useful. If so, it provides a model for providing training in an era of tight travel budgets.

████████ (████████):

No. Need to raise the question first, and then get the right training to address the question.

████████:

-Increase the ability to analyze the raw data.

-Use proprietary software now. Training in SAS and statistics would be good.

-Between the societies we belong to, Staff College, and █████ there are enough training opportunities. It's just funding it in the past few years is the issue.

████████:

-Need training on translational science. Need to be brought up to speed on current research.

-Important that Center maintains training budget. Regulatory personnel need to go out to different institutions so that they can bring ideas back in. It would be devastating if that was discontinued. Chemists should go to meetings outside FDA with industry and risk assessment institutions.

Would like to see more training/seminar events concerning how the review process is done and the related regulations and guidance so that research scientists can figure out what can be done to support the reviewers and how to develop good projects. As an example, this interviewee could not answer most of the questions in the survey because she was unfamiliar with the workings of the review process (even though she has tried very hard to figure it out).

-Nanotoxicology and mixture toxicology needs money for equipment and training. Also needs money for travel to go to best laboratories where people are working in these areas for training.

-Short-term details required every two years for a month or two to learn the regulatory aspect. And vice versa, regulatory scientist works in the lab. In the long term it would be beneficial for the staff (regulatory and research scientists) and the Agency. This would also be good for professional development.

████████:

Hands-on training is passed down. Can't get this through a lecture series.

-Get people out to see what is out there: should be encouraged to participate (submit abstract) when they go to meetings and/or to present their findings when they get back. There should be a focus when they go; there is not much follow-up.

-It is difficult to determine a "mission critical" meeting

████████:

We have extraordinarily good opportunities, but they are not always shared well.

-Don't do enough to bring in/partner with professional societies, rather than going there.

-There is a strong commitment to support training, attend key professional meetings (even if just one meeting)

- Can get training at conferences. Can take training for a future topic not necessarily focused on daily work but might impact on future developments.

-Yes. It goes beyond what we ask for. We can be involved in training and not necessarily for just what we are

working on. Can broaden our scope and enhance interactions with others.

-Yes. More than adequate for training in doing the job, as well as beyond to areas of interest.

-It depends on the money. It is currently hard to go to any meetings, both financially and because you sacrifice work here. Have some internal meetings now. Would be good to expand access to other centers via webinars or Adobe Connect. Because [REDACTED] is a small center, might be able to afford more if the training were made available FDA-wide (e.g., risk assessment).

-More hands on training when new technology comes around.

-I would stress topics on quality assurance and quality control. There should be a quality control person in each Division to take some of the load off the supervisors.

## **Staff College**

-Staff college is good for basics, but not for cutting edge science.

-Collaborated with staff college on a course for genetic epidemiology that was well attended, but did not fall under the category of toxicology. [not everyone may be aware that staff college will support science courses)

-The staff college seems to be focused on management & leadership, but not science (only nanotechnology).

-Staff college is good for business, personal development.

-Staff college: the courses are great, but are not really specific to the work we do.

-We need to ensure that our staff understands what our staff college does. The staff college can help to identify training programs or design training programs, etc. Do not think it's clear to the review scientists that we can call the staff college if we need for this type of training. Can we work together to put this together? Can you find us a class? So in general that needs to be clarified that the staff college is there to help us.

-Our Staff College does a good job on personal development.

-CFSAN Staff College is not as robust as CDER's or others. Maybe if they Joint Staff Colleges. Now others offer courses, but only after their slots are filled by their people first. Should be opened up; increase class size so all reviewers get that type of training on a routine, periodic basis.

## 5b. Are there outside entities we could partner with for more training opportunities?

### Other Agencies

USDA and CDC for statistics training.

-We've had guest seminars from NTP, NIEHS, NCTR, but have had poor turn-out.

-Maybe an overall manager of the scientific process (e.g., for toxicologists) who will stress the importance of training and defend their spending time on this).

- Purdue for botanicals, but can't travel there; have contracts with U Miss Access to NIH classes, maybe EPA risk assessment classes. IARC.

-CVM, CDER

-OPM training in Shepherdstown, but too expensive. USDA Grad School

### Academia/Associations

-Academia is more likely than private corporations for familiarizing with new equipment/techniques.

-Chemical Risk Assessment: [REDACTED] has sponsored risk assessment classes that are of value; Harvard School of Public Health has excellent courses. It's costly but there are good training opportunities.

-UMD to make the most of funds.

-TERA (Toxicology Excellence for Risk Assessment, ACT (American College of Toxicology)

UMD offers courses on nanotechnology and materials science, but we are not encouraged to attend.

[REDACTED] - relatively easy

-American College of Toxicology (ACT) courses are available.

-The American Chemical Society (ACS) has some programs; if we could collaborate with them and get a group rate that would be nice. Some course topics: current trends in equipment and research, toxicology for chemists, risk assessments. A benefit of external training programs is that you are classmates with people from different areas (industry) so you can understand how they approach things versus our regulatory side. This is valuable in itself.

-American Association for Veterinary Medicine. American Association of Pharmaceutical Scientists.

-The Society of Toxicology offers a program where well-known toxicologists give guest lectures in various locations for basically a minimal fee. The Society Toxicologic Pathology has a similar program.

-American Society for Quality.

### Industry

IFT (Institute for Food Technologies)

On-site visits to food facilities (e.g., Hershey, poultry plant, paper recycling)

-Industry has workshops to run equipment that would be nice to check

Hamner Institute.

ILCI (International Life Sciences Institute): partially funded by industry, so avoided, but they do have educational presentations. These groups should be considered as training resources because they are keeping many of the discussions on emerging issues going.

--Revisiting lab techniques/methods via sabbatical program (10-yr rotation) outside Federal government that is long enough to be of value.

-Society for Risk Assessment, Virginia toxicological training

-Various food safety institutes, maybe food law institutes/working groups. Believes we may not be looking into some of these areas for fear of looking as if we don't know anything. Alternatively, we could go out and give talks to these groups.

-Established organizations like IFT, ACS set up courses for at meetings, but if budget allowed could tailor more to FDA.

-Problems with COI. Can't give a talk because of COI, even if we can get money; can't present yourself as an expert in your field.

-It would be advantageous to have the opportunity to see what is going on from the industry side. Example: If you did a lot of work on chemicals is plastics, then go to the plastic industry to see their labs and their factories.

[REDACTED]:

-Yes, there are many testing labs or nonprofits that we could partner with.

[REDACTED]:

-When first got to FDA, training for analytical chemist was offered by industrial groups.

[REDACTED]:

In order to be less reactive to the actual technologies we need to attend a lot of industry/academic sponsored symposia, meeting, and workshops. Don't think attending those things biases us so we can't evaluate the data.

### **Expand in-house**

-We can go outside for training, but there are great scientists here. Need more opportunities to allow exchange of personnel (e.g., do details in the lab). Review scientists can get to know what's new and establish connections for help with methods. Lab would get to know more about the regulatory side. Need more inter-change.

-NCTR

-In the past a [REDACTED] team went to CDER to give training on reproductive toxicology to aid in re-assessing toxic endpoints.

-Develop a course using internal expertise. External training may not be needed if they assessed what they have internally.

-Academic vs. basic vs. applied are very different and outside training might not be that useful.

-There are experts in PK and PBPK profiling at CDER as well as the academic community.

-More cross-training. Consider the idea that after 5 years you have to do a detail in another area.

### **Other**

ACS: seem more drug focused.

[REDACTED]:

-Formerly "Grand Rounds" training brought experts from outside to address a particular issue. These would be good options if funds are available.

[REDACTED] ([REDACTED]):

Workshops would be helpful; for example the Society of Toxicologic Pathology workshop at NIH was very helpful.

-Engage more with academia, EPA, and NIH.

[REDACTED]:

-CDER runs many courses and lectures but there seems to be little awareness of CDER staff college opportunities at CFSAN.

[REDACTED]:

We would always welcome more international communication. The companies would like that. The more harmonization we could do with the review process and approvals would make everyone's life easier, especially for international trade.

## 5c. How can we better ensure professional development needs are being met to ensure development and retention of qualified scientists?

### Inc. opps for adv.

- Good for development as a regulatory specialist, but not a scientist.
- Need a formalized system of documenting personnel issues, such as being discouraged from collaboration when you feel it is unfair, to be discussed upwards.
- Retention comes down to personality; development depends on personal goals. Supervisors have significant impact on advancement and job satisfaction. With a good supervisor, you feel as if you can advance and you are being acknowledged; you will get training.
- Limited opportunities for advancement after you reach Level 13. The job opening doesn't come available very often; may need to wait 10 years. You need to be an expert to qualify for advancement, but are encouraged to be a generalist. Opportunities differ significantly from supervisor to supervisor.
- Need to establish a long-term plan to be ready for advancement. Development is up to your supervisor, and they may not encourage you because it means work for them; therefore, you need to demand to go to meetings, etc. if they don't encourage you to do so. Not even encouraged to go to meetings in areas on which you are an expert; therefore, no recognition as a scientist.

████████:

- Diplomat certification should be encouraged
- One thing we overlook is career goals. There needs to be added emphasis on career development. We pay lip service to it but it has to become a reality. People have to feel when they come here that learning is ongoing. Some of the people at the top who are risk managers really don't seem to care, they just want to turn out a product.

████████:

- Lack of opportunity for growth.
- Not given opportunities to try other things.
- As the only person who does a given job, you can't be assigned to details. Believes ██████████ does a better job of encouraging growth, giving opportunities, promoting from within.

████████:

Scientists need to be able to reach out to managers outside their immediate line of command.

████████:

- Within there are professional development opportunities for some professions.

████████:

There are different promotion/retention policies across the agency, and this is a big problem. Some have a peer review process, some don't. There are different retirement benefits, which allow employees to cherry pick.

-We often lose statisticians. Previously lost toxicologists and pharmacologists to other programs, but now there are retention bonuses. ██████████ promotes based on peer review; there is a conscious effort to promote. Other parts of the system: virtual meetings, work from home, work from distance, flexible hours, training. Collaboration opportunities--all go to retention. But also need to feel contact with the group/feel supported. It has to be a good place to work.

-Requalification checklist/career development plans-identify the training that you need to keep up with.

-Provide more opportunities for promotion. CDER, CFSAN can promote without peer review, but ██████████ does not. People leave ██████████ to get to Levels 14/15 because it is so difficult here.

### Expand Staff College

### Increase training

- Now it is up to you to stay up-to-date. Don't know when/if training money will be available; and when it is, you can't go outside the area.
- More diversity in professional scientific classes offered.
- Some reviewers have no research experience. Could be enhanced by experience with the lab, but they can't come in short-term and learn: need to be committed to a long-term assignment with specific objectives within a specific timeline.
- Details at least year in length, maybe to NIH to learn techniques or to major institute for courses: Johns Hopkins



Should have ongoing committees to set up training in all these new areas. We need to make these people feel their training is appreciated. Give them the opportunity to renew and maybe even teach some of these classes if they have the expertise.

- Development and Retention of Qualified Scientists means recognition of advanced skills as something of value. Management generally prefers loyalty and compliant behavior to advanced knowledge ("I don't understand what he's talking about ...") and questioning. FDA's Peer Review systems are generally avoided and blocked by management, since it allows employees to determine when they (as individuals) believe that they have acquired sufficient expertise to apply for peer review promotion - without management. Mandatory use of the Peer review system for promotion of scientists to non-management positions would give additional support to employees seeking additional training / development opportunities. If management *could not* promote "preferred" employees without going through Peer Review, "preferred" employees would have to work harder to get promotions and managers would have to offer more opportunities for additional training / development.

-Retention of scientists is not a priority. Development is your own strive. You have to be your own squeaky wheel. Also think it's the "skilled" manager's responsibility to be aware of the expertise they have in their group and be aware of the expertise they need in their group, and allow related expertise to develop. They should identify the people they want to become the subject matter experts.

-Recognizing the qualified scientists, helping them move to other positions, and offering them opportunities. Offering specific training so they can move up. Now the focus is on the group, but should not forget the individual.

## Regular surveys

Do a survey every couple of year to see what people want (way of making sure this gets past a manager who isn't helpful).

-Review how many left the Agency and why. Where did they go? If they retired, was it premature?

-Get feedback from employees: do they want to stay? Do they get the training they need?

-The PMAPs are available for each employee. We are asked to review our supervisors and Centers. Like this. The last time around asked for input from the employee on their supervisors and Centers; felt like you could voice your opinion. Feel like some of those have been implemented. If we could does those more regularly it would be nice.

## Exit interviews

## Money/incentives

Bonus program (retention bonus). Are these available to some and not others?

-Retention of qualified scientists is mostly a money issue.

-For retention, satisfaction is based on salary/incentives. They are not consistent across the centers.

-Retention: better remuneration, more fare distribution (CDER gets more money, industry). CSOs get better raises than scientists and have more opportunity for advancement; scientists need to wait for someone to retire or can go through expert review process, but this requires a lot of research/presentations. There are a limited number across the agency.

## Other

-When mistakes are made, there is no buffer, so that the person is kept down or kicked out, even though they may be a very good scientist.

-Micro-management structure is discouraging to many scientists. -Morale is a big problem. Leadership training is not very effective. Reviewers are not encouraged to attend.

-More involvement in regulatory decisions; set this as a personal goal; additional support from the Agency.

-Participation in interesting topics (aspartame, olestra, melamine, WHO initiatives); learn the facts about the substances and how various disciplines interact. You can take that information back to your group.

-Management/leadership doesn't have a strong interest and commitment to science-based decision making. This would change how scientists feel.

-Allow them to do their own research in addition to work.

-Everyone needs to do their part: Reviewers need to speak up; supervisors need to be aware of the needs of their staff and push up the chain for resources. Need to be creative with solutions: bring someone in to train a large

group rather than send people out. Staff college is very good with working with them to develop training.

[REDACTED]:  
We need to develop a better way of determining who is going to be a manager. At the moment it is a haphazard approach. We need more open-thinking about toxicology at the top--a willingness to say hey, I don't understand everything, I want to defer this to somebody else. Also must listen to people in the trenches.

[REDACTED]:  
-Recommended training hours per year or expectations to publish new findings or current publish.

[REDACTED]:  
-Have designated supervisors. To ensure professional development, need a supervisor that you are comfortable talking to. Then you know the rules and regulations. Right now there is a lack of guidance. Need a well-structured office so that you know the chain of command.

[REDACTED]:  
-We do have a professional peer review process for upper level people which is intended to address that. The problem is that people don't necessarily know what others are doing to be professional peer reviewers, but don't know if you can do any better.

-The practice of promoting regulatory toxicologists without peer review should be reconsidered. Peer review should be focused on expertise in a specific area of toxicology. While this will not automatically include a research component, it does create a mechanism that encourages review toxicologists to seek out and collaborate with lab toxicologists or others to push the field of toxicology forward and be true experts with the outside recognition that is the usual criterion for promotion to GS 14 and 15.

-Performance evaluations for review toxicologists should make explicit reference to collaborative efforts in research and new toxicology method implementation as one possible route to exceeding expectations in at least one performance element.

-Regulatory review toxicologist should be allowed the same sort of professional development time allotted to MDs and Pharmacists to allow them to participate in collaborative projects with lab toxicologists or other innovative projects inside or outside of CFSAN. Successful collaborations should be rewarded via promotion via peer review

[REDACTED]:  
-Pretty impressed with [REDACTED] and the open-mindedness of management. [REDACTED] needs to encourage people to develop their own interest, and to be more transparent in how things are going. [REDACTED] seems to be trying hard to do that.

-Retention: too many administrative duties. Maybe a division of editors to assist: FOI Summaries could be done more efficiently, too much focus for scientists on formatting issues. It's like doing your review twice.

-We are not going to be able to lure people to the Federal government because of money. We will have to lure people because of the mission and work environment we provide. Most scientists want to keep up to date; if we can find a way to do that and still work here then we will be able to keep more people.