SENATE APPROPRIATIONS COMMITTEES SIGNIFICANT ITEMS

SENATE COMMITTEE REPORT (115-259)

5. 1. Animal Feed Ingredients

The Committee is concerned with the slow pace of review and approval of ingredients for feed for animals. The Committee urges FDA to dedicate additional personnel to speed the review and approval process.

FDA Response:
FDA's budget authority currently allocates 12 full-time equivalents (FTE) to work on animal food ingredient review. These positions work across the vital review areas of target animal safety (i.e., safety of the animals eating the food ingredient), safety of the human food derived from food-producing animals, manufacturing of the animal food ingredient, functionality of the ingredient, and communication with the ingredient manufacturers during the review process. FDA has done considerable work to enhance the efficiency of the review process, but the number and complexity of submissions have increased dramatically. Submissions of Food Additive Petitions (FAPs) have gone up by 150 percent in the last four years and submissions of Generally Recognized As Safe (GRAS) notices have gone up by 200 percent in the last year. FDA analyzed the resources needed to meet performance goals and statutory requirements and is requesting funding to hire more personnel to speed up the review process and stay current with the science.

2. Breast Density

The Committee recognizes the importance of patients receiving their own personal medical information and directs the Food and Drug Administration to ensure that mammography reports and summaries received by patients and their providers include appropriate information about breast density specified by the Secretary, including, at a minimum, the effect of breast density in masking the presence of breast cancer on a mammogram, the qualitative assessment of the provider who interpreted the mammogram, and a reminder to patients that individuals with dense breast tissue should talk with their providers if they have any questions or concerns about their summary.

FDA Response:
The Agency agrees with this Committee. FDA is committed to ensuring that mammogram lay summaries and medical reports provided to patients and their healthcare providers contain the information they need to make informed health care decisions. To further this goal, FDA has drafted proposed amendments to the implementing regulations of the Mammography Quality Standards Act of 1992 that, among other updates, address breast density reporting, and plans to publish the proposed rule in early 2019.

3. Cancer Immunotherapy Clinical Trials

The Committee is aware of the remarkable promise of cancer immunotherapy and encouraged by the FDA's recent approval of new treatments that harness this approach to fighting cancer. More than 1,500 immuno-oncology clinical trials are in some stage of development. As more patients turn to immune-based treatments, and more clinical trials are conducted to evaluate them, understanding how to recognize and manage the side effects of cancer immunotherapies will become increasingly important. Currently, however, standard parameters for reporting cancer immunotherapy-related adverse events in clinical trials are lacking, and this makes comparisons and management across studies challenging. The Committee, therefore, urges the FDA to work with the research community and the pharmaceutical industry to develop standardized templates for reporting toxicities in cancer immunotherapy clinical trials.

FDA Response:
The Oncology Center of Excellence (OCE), along with FDA's Center for Biologics Evaluation and Research and Center for Drug Evaluation and Research, is currently engaged in developing standardized templates for reporting toxicities in cancer immunotherapy trials, as noted below.

- OCE is leveraging the experience within FDA in review of cancer immunotherapeutics, including immune checkpoint inhibitors (ICI) with over 2000 clinical trials evaluating ICIs and nearly 50 new or supplemental FDA approvals in oncology across seven approved ICIs, to provide recommendations for standardizing templates for the identification and reporting of toxicities in cancer immunotherapy trials.
- OCE has an immune-mediated toxicity working group that is addressing key concerns for standardization of identification and management of immune-mediated adverse reactions (imAR) with immuno-oncology products.
- OCE is engaging with multiple stakeholders including the research community, professional societies, patient advocacy organizations, and the pharmaceutical industry on identification, management, and reporting of cancer immunotherapy-related adverse events in clinical trials and in the post marketing setting.

4. Computational Medicine

The Committee appreciates FDA's continued support for and use of modeling and simulation in clinical trials, as well as its work toward the establishment of an affiliation agreement with an academic institution with expertise in this field. This partnership will allow for the development of personalized medical interventions, optimizes the regulatory process with in silico clinical trials and bridges gaps in the current regulatory infrastructure. The Committee directs FDA to formalize this important function in improving outcomes and reducing costs inherent to drug and device discovery.

FDA Response:
Modeling and simulation can be valuable tools deployed throughout medical product development and review, for example, to estimate and evaluate appropriate doses, to help design efficient clinical trials, and to predict and assess product safety. They can also help to explain

variable patient response and provide an alternate path forward in challenging areas where there may be an unmet need or small patient population. FDA is committed to advancing both important methods.

Application of clinical trial simulations and predictive or mechanistic safety evaluation for advancing drug development have been identified as priority areas under the model informed drug development (MIDD) Pilot Program. FDA committed to develop the MIDD Pilot Program as part of the performance goals associated with the Prescription Drug User Fee Act (PDUFA VI), included as part of the FDA Reauthorization Act of 2017. FDA announced the Pilot Program on April 16, 2018. This program provides an opportunity for drug developers and FDA to discuss the application of MIDD approaches to the development and regulatory evaluation of medical products and to provide advice on the use of particular MIDD approaches in a drug development program. Under this pilot, FDA will accept 2-4 paired-meeting requests quarterly each year throughout the PDUFA VI period where selection will prioritize requests that focus on dose selection or estimation, clinical trial simulation, and predictive or mechanistic safety evaluations. So far, FDA has granted paired-meeting requests to 6 sponsors that are applying modeling and simulation approaches to inform the ongoing drug development. Additionally, FDA co-sponsored a public workshop with the International Society of Pharmacometrics on Model-Informed Drug Development for Oncology Products in February 2018. Meeting participants discussed best practices in integrating data of all kinds (pharmacokinetics, pharmacodynamics, efficacy, safety) into models, novel imaging techniques and biomarkers, and potential regulatory implications of model-informed decisions in drug development. This is the first of four workshops FDA plans to hold to help identify best practices for MIDD. FDA will also develop and revise relevant existing guidance on MIDD.

In addition, FDA is committed to advancing the use of complex innovative trial designs and has launched several efforts to fulfill commitments outlined in PDUFA VI. The scope of the efforts includes, but is not limited to, complex adaptive, Bayesian, and other novel clinical trial designs, with a focus on designs for which simulations are necessary to evaluate properties of the trial. Such designs hold the promise of increasing trial efficiency and providing an alternate path forward in challenging areas where there may be an unmet need or small patient population. In March 2018, FDA convened a public workshop on complex innovative trial designs that included a panel of expert academicians. Moreover, FDA launched the CID Pilot Meetings Program on August 29, 2018. Under this program, FDA will grant sponsors of proposals accepted into the Pilot Meetings Program two meetings with the FDA to discuss the planned clinical trial design and analysis including simulations. To further promote innovation, FDA may present the trial designs developed under the pilot program as case studies, including trial designs for drugs that have not yet been approved. In September 2018, the FDA also published a draft guidance on adaptive designs to better guide pharmaceutical companies on the use of such designs.

For medical devices, FDA continues advancing these methodologies and techniques to best take advantage of the benefits for continued product innovation and more rapid introduction of life saving technology to U.S. patients. For instance, FDA has demonstrated that the Virtual Patient Model can serve as one framework for in silico clinical trials and created a virtual population to enable computer-based simulations for medical devices. This allows CDRH to harness data from computer-based simulations to augment clinical trials, i.e., an in silico clinical trial. As an

example, CDRH has completed a fully in silico replication of a pivotal trial submitted as part of the PMA for a novel breast cancer imaging system (for new digital breast tomosynthesis systems). The successful completion of this pivotal in silico trial is now publicly available through a recent publication in JAMA[124] and will provide industry and others with the tools for performing fully in silico clinical trials for imaging systems, which will greatly minimize cost and radiation exposure for patients and help to assure devices meet our gold standard to come to market.

CDRH also currently partners with the University of Mississippi Medical Center (UMMC), using its sophisticated in silico models to predict how interventions, such as renal denervation, can affect certain patient populations. This partnership will build upon UMMC's robust model to evaluate the impacts of drugs and devices across the entire body, to project the long-term effects of particular treatments and interventions and study the ways in which drugs and devices might impact populations differently.

Regulatory evaluation of modeling and simulation is advancing alongside the power and sophistication of the tools. Therefore, FDA formed an Agency-wide working group on modeling and simulation with objectives that include aligning regulatory decision-making with modeling and simulation, and, where appropriate, employing in silico clinical trials. Completing these objectives will advance the in silico clinical trial framework for the medical product Centers and help clarify appropriate methods and guidelines for in silico clinical trials.

As noted, FDA employs a broad range of modeling disciplines, including mechanistic-based, chemistry-based, physics-based, exposure-based, biological, and statistical models. These techniques can also enhance the mechanistic understanding of disease progression and the complex interplay between genetics and predictive biomarkers with response to therapy. FDA will develop guidance and standards related to use of modeling and simulation in device and drug development and evaluation to continue such advancement, which is critical to enabling safe and effective medical products to continue coming to market.

5. Cotton Ginning

The Committee is concerned about the impact of the ''Current Good Manufacturing Practice, Hazard Analysis, and Risk-Based Preventive Controls for Food for Animals'' final rule (80 FR 56170; September 17, 2015) on the cotton industry. The Committee notes post-harvest activity of ginning cotton does not transform the resulting cottonseed into a ''processed food,'' and thus, cottonseed should fall within the definition of a ''raw agricultural commodity'' for purposes of rules promulgated pursuant to the FSMA. In addition, the Committee is concerned about the rationale for the definitions of ''primary production farm'' and ''secondary activities farm'' and how these definitions factor into the determination of operations either being exempt from or covered by certain requirements of the final rule. Therefore, the Committee directs the FDA to

[124] JAMA Network Open. 2018;1(7):e185474. doi:10.1001/jamanetworkopen.2018.5474

provide outreach and technical assistance to cotton ginning operations to assist them in complying with the final rule or subsequent guidance documents.

FDA Response:
FDA is aware of the cotton ginning industry's concerns regarding whether certain entities are classified as farms or facilities. The Agency also is aware of their concern related to whether ginning results in a "processed food." In January 2018, FDA announced its intent to pursue rulemaking related to the farm definition and will consider the concerns of the cotton ginning industry in that evaluation. The Agency also announced its intent to exercise enforcement discretion with respect to application of the ''Current Good Manufacturing Practice, Hazard Analysis, and Risk-Based Preventive Controls for Food for Animals'' (PCAF) regulation to facilities that would be considered secondary activities farms except for the ownership of the facility, which would include certain cotton ginning entities. The Agency intends to continue the exercise of enforcement discretion until it is able to address cotton industry concerns through additional rulemaking or by other means. See Policy Regarding Certain Entities Subject to the Current Good Manufacturing Practice and Preventive Controls, Produce Safety, and/or Foreign Supplier Verification Programs: Guidance for Industry at https://www.fda.gov/downloads/Food/GuidanceRegulation/GuidanceDocumentsRegulatoryInformation/UCM590661.pdf.

FDA has had multiple meetings with the cotton ginning industry on this topic. In October 2017, FDA staff participated in an educational tour with representatives from the cotton ginning industry, cotton farmers, the Alabama Department of Agriculture and Industries, and Rep. Robert Aderholt's office.[125] During the meetings with the industry and the educational tour, FDA reiterated its commitment to resolving the industry's concerns about the applicability of the PCAF rule to ginning operations. Since that time, FDA formalized its commitment by releasing the January 2018 enforcement discretion guidance for industry ("Policy Regarding Certain Entities Subject to the Current Good Manufacturing Practice and Preventive Controls, Produce Safety, and/or Foreign Supplier Verification Programs"). Since the issuance of the guidance document, FDA has responded to requests for status updates from the cotton industry and remains committed to providing additional information on the status when more information becomes publicly available.

6. FSMA Clarification for Small Farms

The Committee directs the FDA to provide further clarification to small farms on the requirements for compliance with the Food Safety Modernization Act, including information on the qualified exemptions available to small and very small farms and the actions required to achieve compliance under these exemptions. The Committee also urges the Food and Drug Administration to communicate with (including through appropriate guidance) and offer technical assistance to assist small farms with compliance.

FDA Response:

[125] https://blogs.fda.gov/fdavoice/index.php/2017/11/talking-fsma-in-the-land-of-cotton-and-looking-for-middle-ground/

FDA is committed to ensuring that farms, in particular small and very small farms, have the assistance they need to understand and comply with the rules issued under the FDA Food Safety Modernization Act (FSMA). In September 2017, FDA issued a small entity compliance guide on the FSMA Produce Safety Rule, intended to assist small and very small farms to better understand the rule. The guidance provides the definitions for small and very small businesses and explains the qualified exemption provision. Thus, the small entity compliance guide can help farmers determine whether they are eligible for a qualified exemption, which would modify the requirements they are subject to under the Produce Safety Rule. In addition, FDA has issued small entity compliance guides for the current good manufacturing practice, hazard analysis, and risk-based preventive controls regulations for both human food and animal food that can help small and very small farms that also engage in on-farm manufacturing and processing.

FDA has engaged in other activities intended to provide technical assistance to farmers on the requirements of the Produce Safety Rule and how to comply. In October 2018, FDA issued a draft compliance and implementation guidance to assist farmers in meeting Produce Safety Rule requirements. To further assist farmers and other stakeholders, we published "At-A-Glance" overviews that highlight the key points in each chapter in the draft guidance. The draft guidance document is open for public comment for 180 days. FDA also held four public meetings around the country at which the Agency had an opportunity to engage with stakeholders on the Produce Safety Rule draft guidance. In addition, the FSMA Technical Assistance Network is a central source of information for questions related to FSMA rules, programs, and implementation strategies, including for small and very small farmers, who have questions on complying with the Produce Safety Rule. FDA—along with USDA and Cornell University—created a Produce Safety Alliance (PSA) to develop and deliver training on the Produce Safety regulation requirements that would be of particular assistance to small and very small farms. PSA training courses have been available since Fall 2016. FDA also awarded a cooperative agreement, called the Local Food Producer Outreach, Education, and Training to Enhance Food Safety and FSMA Compliance Cooperative Agreement, intended to address small entities, in August 2016. The cooperative agreement is intended to develop and provide science-based, culturally-specific food safety training, education, and outreach for local food producers and processors.

7. FSMA Cooperative Agreements

The Committee is aware that some states that have entered into cooperative agreements under the State Produce Implementation Cooperative Agreement Program to provide education, outreach, and technical assistance have or are considering changing the state agency responsible for implementing these agreements. The Food and Drug Administration is directed to work with any state that designates a new implementing agency to ensure it can continue to receive funding under existing cooperative agreements without delay or loss of funding.

FDA Response:
The funding opportunity announcement (FOA) for the cooperative agreement "State and Territory Cooperative Agreement to Enhance Produce Safety in Preparation of Implementation of FDA's Rule: Standards for the Growing, Harvesting, Packing, & Holding of Produce for Human Consumption" (PAR 16-137) includes language allowing funding to be provided to the agency

with state legislative and/or regulatory authority to implement the Produce Safety Rule adopted in accordance with the FDA Food Safety Modernization Act and to provide education, outreach, and technical assistance for the rule.

If another agency is granted said authority, it is permissible under applicable regulations covering federal grant funding and under the HHS Grants Policy Statement to change the implementing agency awarded the funds upon the submission of a change request and subsequent review and approval by the grant funding agency. Doing so, per established regulations and the HHS Grants Policy Statement, results in the state or territory continuing to receive funding without delay or loss of funding.

8. Human Drug Review Committee

The Committee strongly encourages the FDA to fully utilize its authorities under 18 U.S.C. 208(b)(3) to include no less than two members with an expertise in the indication for which the drug is meant to treat on each Advisory Committee when that Committee is reviewing a drug that has been designated an Orphan Drug.

FDA Response:
Advisory committees play an important role in FDA activities to protect and promote public health, and provide FDA with independent advice on scientific, technical, and policy matters related to the development and evaluation of FDA-regulated products.

FDA agrees with the intent suggested by the Committee and is diligent in trying to get experts in the relevant disease to participate in each advisory committee meeting. It is valuable to have several such experts at the meeting, as each may bring a different perspective on important scientific, technical and policy matters.

On the other hand, FDA is committed to adhering to the laws and regulations governing the process for selecting advisory committee members, which are intended to help minimize bias and potential conflicts of interest. FDA for many years has screened, prior to each advisory committee meeting, all potential participants who are Special Government Employees (SGEs) or regular Government employees, to determine whether the potential for a financial conflict of interest exists. Where such a conflict exists, the agency may grant a waiver allowing participation in an advisory committee meeting when statutory criteria are met; for example, when the need for the individual's services outweighs the potential for a conflict of interest created by the financial interest involved (18 U.S.C. 208(b)(3)).[126] FDA works diligently to have two or more individuals with an expertise in the indication for which the drug is meant to treat on each advisory committee; however, in some cases it is not feasible given the statutory constraints. FDA will continue to work on this matter and consider the committee's suggestion within the statutory framework.

[126] Guidance for the Public, FDA Advisory Committee Members, and FDA Staff on Procedures for Determining Conflict of Interest and Eligibility for Participation in FDA Advisory Committees. https://www.fda.gov/oc/advisory/waiver/coiguidedft.html

9. Misleading Maple Marketing

The Committee is concerned about the explosion of products marketed using the word maple and related iconography, which intentionally misleads consumers who perceive the use of the word maple and related iconography to mean that a food product contains some measurable quantity of maple syrup to flavor or sweeten the product, which consumers identify as a characterizing ingredient. The Committee directs the FDA to perform a detailed analysis of consumer perception of foods marketed with the word maple or related iconography.

FDA Response:
FDA shares the Committee's concern for the truthful labeling of products and the importance of having consumers be able to make informed choices about their foods. Current regulations allow use of terms like "maple," "maple-flavored," or "artificially maple-flavored" on the food label without having any maple syrup in the product if it contains maple flavoring. The Agency's website includes information to help educate consumers about these regulations and the differences in the ways that ingredients and flavors are declared on product labels, including use of the terms "maple" and "maple syrup." That consumer update is available at www.fda.gov/ForConsumers/ConsumerUpdates/ucm521518.htm.

FDA has conducted a preliminary review of potential consumer perception issues and has met with representatives of the maple syrup industry regarding the applicable labeling regulations. The Agency is happy to continue meeting with industry representatives to discuss available data and other industry information on consumer perceptions regarding maple and maple syrup that may complement our own monitoring of the issue. FDA will consider taking action against products that are misbranded, as appropriate, consistent with our food safety priorities and resources.

10. Olive Oil

Because of the substantial interest in and consumption of olive oil throughout the United States, driven in part by the significant scientifically-confirmed health benefits of these oils and the fact that the United States has become a globally-important producer of olive oils, especially extra virgin olive oil, the Committee directs the FDA to establish a separate U.S. Standard of Identity for different grades of olive oil (e.g. refined, virgin and extra virgin) and olive-pomace oils. The Committee is particularly concerned with the number of different state standards for olive oils in the U.S. Because the health benefits of olive oil vary by grade, it is important to establish a uniform set of the standards to better inform and protect consumers. Extra virgin olive oil is the highest quality of olive oil and provides the greatest health benefits for consumers. The FDA is directed to consult and meet with domestic producers and importers of olive oil to develop a science-based Standard of Identity for extra virgin olive oil and olive oil best suited to ensure the integrity of these products for U.S. consumers.

FDA Response:

Under FDA's Nutrition Innovation Strategy, the Agency is working to modernize the framework for standards of identity with the goal of maintaining the basic nature, essential characteristics, and nutritional integrity of food products while allowing industry flexibility for innovation to produce more healthful foods. To support this effort, FDA has indicated its intention to reopen the comment period on a proposed rule seeking to establish general principles to update the framework for standards of identity. While FDA is working hard on this comprehensive effort to modernize food standards, the Agency is proceeding with ongoing work on standards and labeling consistent with our priorities and resources.

FDA is currently reviewing a citizen petition related to olive oil. The petition was submitted in 2012 by the North American Olive Oil Association (Docket No. FDA-2012-P-0754) and requests FDA to develop a standard of identity for olive oil and olive pomace oil that includes compositional standards and analytical testing. No final decision has been made on this petition. In October 2018, FDA met with olive oil producer Deoleo SA to discuss their interest in a standard of identity for olive oil. FDA would be happy to have further dialogue with the North American Olive Oil Association and other industry representatives to discuss this matter.

11. <u>Opioids</u>

The Committee continues its directive for FDA to refer any drug application for an opioid to an advisory committee for their recommendations prior to approval, unless the FDA finds that holding such advisory committee is not in the interest of protecting and promoting public health.

The Committee directs the Commissioner to seek recommendations from the Drug Safety and Risk Management Advisory Committee regarding a framework for the inclusion of information in the labeling and/or REMS of drugs that are opioids or used in Medically-Assisted Treatment relating to the co-prescription of opioid overdose reversal drugs along with opioids prescribed to patients that meet CDC guidelines as at risk for overdose.

FDA Response:
FDA will continue to follow section 106 of the Comprehensive Addiction and Recovery Act (CARA) concerning advisory committees. Specifically, FDA will convene an expert advisory committee before approving any New Drug Application for an opioid unless FDA determines that such referral is not required, as provided in CARA section 106(a)(1)(B) ("Public health exemption"). FDA held 11 opioid-related advisory committee meetings in 2018.

FDA recognizes that emergency treatment of known or suspected opioid overdose is an urgent public health priority, and to advance these efforts, there is still a need to improve access to naloxone. On December 17-18, 2018, FDA held a two-day advisory committee meeting to solicit input and advice on strategies to increase the availability of naloxone products intended for use in the community. FDA asked our external advisors from the Anesthetic and Analgesic Drug Products and the Drug Safety and Risk Management Advisory Committees to consider various options for increasing access to naloxone. This information will help us weigh logistical, economic, and harm reduction aspects of different strategies, and FDA will consider whether naloxone should be co-prescribed with all or some opioid prescriptions to reduce the risk of overdose death.

12. Polypharmacy

The routine usage of five or more prescription medications within the same period is becoming increasingly prevalent among older adults, elevating risk factors for drug-drug interactions and adverse events. The Committee directs the FDA to assess potential impacts of polypharmacy, which might help inform the design of clinical studies.

FDA Response:
As a part of new drug evaluation, FDA routinely assesses the potential for drug-drug interactions. This evaluation considers the potential for drug interactions that result from polypharmacy. The results of FDA evaluations can inform prescription drug labeling that is often used by prescribers, drug information specialists, and clinical decision support platform developers to aid in therapeutic decision-making at the patient level. Additionally, FDA is developing guidance for sponsors on how to evaluate drug-drug interactions (DDIs) during drug development. In October 2017, the FDA published a draft guidance entitled *Clinical Drug Interaction Studies - Study Design, Data Analysis, and Clinical Implications*. This guidance, when finalized, is intended to help sponsors of investigational new drug applications and applicants of new drug applications evaluate DDIs during drug development.

13. Ready To Eat Foods

The Committee is aware that FDA is in the process of finalizing guidance regarding Listeria monocytogenes [Lm] in RTE foods. Reducing incidents of listeriosis is an important health goal and the Committee supports efforts to accomplish this objective. The Committee urges FDA to complete a comprehensive risk assessment to ensure any final guidance document is realistic and fully based in science prior to making any changes to the action level of Lm in RTE foods.

FDA Response:

FDA is careful to ensure that its guidances are solidly grounded in current science and offer flexibility to firms in implementing controls as appropriate to their products, processes, and facilities. In 2008, FDA published a draft compliance policy guide (CPG) for *Listeria monocytogenes* (Lm) stating that the Agency would not consider a ready-to-eat (RTE) food that does not support growth to be adulterated if Lm did not exceed 100 cfu/g. This CPG was not finalized. FDA determines the risk associated with Lm in food on a case-by-case basis depending on a number of factors, including whether the food supports the growth of the pathogen.

FDA has significant scientific expertise in Lm and has devoted substantial effort toward advancing the science in this area, including through risk assessment. FDA, the Centers for Disease Control and Prevention, and the USDA's Food Safety and Inspection Service jointly developed a Quantitative Assessment of Relative Risk to Public Health from Foodborne *Listeria monocytogenes* Among Selected Categories of Ready-to-Eat Foods. The assessment took four

years to complete, beginning with a *Federal Register* notice of intent issued in 1999 and culminating in completion of the final assessment in 2003. FDA continues to gather data and monitor developments in the body of science around the presence of Lm in RTE foods, such as information related to a 2015 outbreak of listeriosis from ice cream that was found to contain very low levels of Lm, and to develop models to characterize the risk of listeriosis in highly susceptible population subgroups.

14. Seafood Advisory

The Committee remains concerned that the FDA published final seafood advice for pregnant and nursing women on January 18, 2017, without going through the necessary interagency review, consumer focus group testing, or the opportunity for the public to comment on the scientific peer review. Therefore, the Committee directs the FDA to reissue the final ''Advice About Eating Fish'' (published in 82 Fed. Reg. 6571 (January 19, 2017)) in a manner that is consistent with the FDA's nutrition science on the net effects of seafood consumption.

FDA Response:
The 2017 final fish advice, entitled "Fish: What Pregnant Women and Parents Should Know,"[127] is based on extensive scientific research and expertise across a range of disciplines, as well as multiple opportunities for public comment and stakeholder input. The 2017 advice reflects the work of experts in a range of disciplines within both FDA and the Environmental Protection Agency (EPA), with assistance and input from the National Institutes of Health and other operating divisions within the Department of Health and Human Services. When updating the fish advice, FDA gave broad consideration to the available research, including FDA's own net effects assessment. This advice went through an extensive interagency review process, as well as an external peer review process. The agency posted a peer review plan for "Technical Information on Development of Fish Consumption Advice" as part of the agency's peer review agenda. Documentation of the technical information and external scientific peer review process is available on FDA's website.[128]

Furthermore, FDA and EPA received and considered more than 220 public comments on the 2014 draft version of the advice; these comments came from academia, industry, nongovernmental organizations, and consumers. In light of these comments and updated research and technical information, FDA and EPA developed a revised method for categorizing fish and conducted an external peer review of the information and method used. In November 2014, the FDA's Risk Communications Advisory Committee held a meeting that addressed the updated draft fish advice in great detail and included presentations by FDA and EPA on the substance and presentation of the draft advice, as well as presentations by invited experts in risk communications. Members of the public were given an opportunity to express their views to the Risk Communications Advisory Committee and to Agency officials in attendance. Documentation of the public and expert input is available at FDA's website. FDA believes this

[127] https://www.federalregister.gov/documents/2017/01/19/2017-01073/advice-about-eating-fish-from-the-environmental-protection-agency-and-food-and-drug-administration

[128] https://www.fda.gov/Food/ResourcesForYou/Consumers/ucm393070.htm

additional information demonstrates the rigor of our process for reviewing and updating the fish advice.

FDA issued denial letters in response to a citizen petition and then a petition for reconsideration requesting that FDA withdraw and reissue the 2017 seafood advice. FDA's response letters, which include information about FDA's consideration of the FDA Net Effects Assessment, are available in Docket No. FDA-2017-P-3196.[129]

15. Sunscreen Labeling Regulations

The Committee remains significantly concerned that the FDA has not approved a new over-the-counter [OTC] sunscreen ingredient since implementation of the Sunscreen Innovation Act, which improved the process by which the FDA reviews sunscreen ingredients and required the FDA to finalize an effective sunscreen monograph within 5 years. The Committee directs the FDA to meet with sponsors regarding the development of a testing regimen for sunscreen ingredients, consistent with current scientific standards, that appropriately balances the benefit of additional skin cancer prevention tools versus the risk of skin cancer. The Committee also directs FDA to maintain funding for agency efforts to clear this backlog of sunscreen applications.

In addition, the Committee is disappointed that FDA has not yet finalized a rule limiting the maximum Sun Protection Factor [SPF] to ''50'' or ''50+'' as directed by the fiscal year 2018 Consolidated Appropriations Act, and as such the Committee directs FDA to finalize the rule immediately. The Committee is also disappointed that FDA failed to issue a proposed rule to establish testing and labeling standards for sunscreen sprays and directs FDA to do so immediately.

FDA Response:
Given the recognized public health benefits of sunscreen use, the FDA is committed to finding ways to help facilitate the marketing of safe and effective sunscreen products that include additional over-the-counter (OTC) sunscreen active ingredients. As noted in the GAO's November 2017 report *FDA Reviewed Applications for Additional Active Ingredients and Determined More Data Needed*, the FDA relies on industry to submit the data needed to make the required safety and effectiveness determinations for each pending sunscreen active ingredient being evaluated under the SIA framework, and in every case FDA has determined that the evidence supplied to date is insufficient to support a determination that a sunscreen containing the active ingredient would be Generally Recognized as Safe and Effective (GRASE).[130]

There is no backlog of pending sunscreen applications. The Agency has identified current data gaps for each active ingredient being evaluated under the SIA framework and communicated them in proposed sunscreen orders and, when requested, granted meetings with active ingredient sponsors. To date, the Agency has not received any additional data from manufacturers for any

[129] https://www.regulations.gov/docket?D=FDA-2017-P-3196

[130] US Government Accountability Office (November 15, 2017). Retrieved November 15, 2017, from www.gao.gov/products/GAO-18-61.

of the pending sunscreen ingredients that were the subject of SIA-required proposed sunscreen orders issued in 2015.

FDA will continue to work with industry and public health stakeholders as it implements the SIA to help ensure that the sunscreens consumers use every day on themselves and their families are safe and effective for daily, life-long use.

To date, FDA has met all statutorily mandated SIA deadlines and remains committed to achieving that goal in the future. As required by the SIA, the FDA is working to finalize effective OTC monograph regulations for sunscreens by November 26, 2019. The Agency anticipates including provisions related to the effectiveness of various SPF levels and dosage forms for sunscreens. In order to finalize such a monograph, FDA intends to first publish a proposed rulemaking on sunscreens in order to provide the opportunity for public comment.

16. White Oak Expansion

The Committee is aware of the need for FDA facilities to accommodate an anticipated expanded workforce due to broader missions related to food safety and other mandates in legislation over the last few years. In the Committee's report for fiscal year 2016, the Committee requested a feasibility study to update and issue a revised Master Plan for land inside and contiguous to the White Oak Campus in order to address its expanded workforce and the facilities needed to accommodate them. The Committee directs FDA to complete this study as soon as possible. Due to the challenging fiscal environment, the Committee encourages the FDA and GSA to consider innovative financing options and partnership opportunities with non-federal government entities that provide reasonable cost options contiguous to the White Oak campus.

FDA Response:

The Consolidated Appropriations Act, 2016, authorized $5,000,000 for FDA to complete a feasibility study to update and issue a revised Master Plan for land inside and contiguous to the White Oak Campus to address its expanded workforce and the facilities needed to accommodate them.

FDA provided the Government Services Administration (GSA) with a $5,000,000 Reimbursable Work Authorization in 2016. Since then, GSA and FDA have collaborated and awarded contracts for development of an FDA Headquarters Housing Strategy/Migration Plan and a new Federal Research Center (FRC) Master Plan for the White Oak Campus. These documents address the feasibility of, and options for, accommodating FDA 's existing headquarters staff that have not yet been consolidated at White Oak, as well as FDA's growing headquarters staff on or near the FRC. On December 6, 2018, the National Capital Planning Commission voted to approve the new FRC Master Plan, which will be implemented in phases subject to the availability of funding. The FDA Housing Strategy/Migration Plan is still under development.

FDA must depend on GSA to satisfy its office housing needs. GSA considered a partnership opportunity proposed by a non-Federal Government entity that provided a leasing option to

enable FDA to maintain very close proximity to its campus headquarters in White Oak, including space contiguous to the White Oak Campus. In response to the proposal, GSA determined that FDA's housing needs first had to be documented through the process of developing the Housing Strategy/Migration Plan before the acquisition of space could occur. GSA also determined that satisfying FDA's housing needs required Congressional prospectus lease authority and that, after Congressional approval, the housing needs would be satisfied through a competitive leasing process. Sufficient progress has been made on the development of the Housing Strategy/Migration Plan to provide the data needed for GSA and FDA to collaborate on a lease prospectus submitted to OMB for FY 2019 approval.