SIGNIFICANT ITEMS

HOUSE APPROPRIATIONS COMMITTEES SIGNIFICANT ITEMS

HOUSE COMMITTEE REPORT (115-706)

1. Food Safety and the Food Safety Modernization Act Funding

The Committee directs FDA to provide information to the public via reports and on its website as it relates to the link between FSMA activities and performance measures, especially as outcome measures support reductions in foodborne illnesses, hospitalizations, and deaths.

Also, the Committee directs FDA to continue their outreach and education efforts to inform the regulated industries how they come into compliance with the FSMA foundational regulations. As previously noted, it is the intent of Congress for FDA to ensure an even playing field in the application of FSMA regulations as it relates to both domestic and imported producers, processors, and manufacturers of food and animal feed. Lastly, the Committee believes that FSMA implementation places additional requirements on state governments and private stakeholders, and therefore urges the FDA to provide sufficient resources to state education and inspection programs to address these needs.

FDA Response:

FDA is developing measures to monitor compliance and industry's implementation of the FDA Food Safety Modernization Act (FSMA) rules. The measures will be categorized by rule and are at various stages of review, prioritization, approval, and implementation. The first set of measures tracks the implementation of the Preventive Controls for Human Food (PCHF) and Preventive Controls for Animal Food (PCAF) rules. A set of PCHF and PCAF measures will be published in early 2019 via FDA's Agency-wide performance management system, FDA-TRACK. The second set of measures to be published on the FDA-TRACK website will cover the Foreign Supplier Verification Programs (FSVP) for Importers of Food for Humans and Animals rule. This set of measures is slated to be released in Spring 2019.

Regarding the reduction in foodborne illness, hospitalizations, and deaths, FDA will evaluate the number of reported outbreaks and estimated illnesses in the U.S. population as measures of the effectiveness of the rules in collaboration with the Centers for Disease Control and Prevention (CDC). The development of additional public health outcome measures related to FSMA activities will be subject to the availability of sufficient data.

FDA is committed to continuing outreach and education efforts to assist regulated industries' compliance with the FSMA rules. Training the food industry is critical to the success of FSMA. To help facilitate training, FDA, together with United States Department of Agriculture (USDA), has funded a network of public and private partners in state, federal, tribal, and international governments, industry, and academia for the development and delivery of training.

The vision of FSMA training began in 2010-2012 with the creation of public-private Alliances funded primarily by FDA as a resource for industry and to facilitate widespread understanding of the new standards to support compliance. The Produce Safety Alliance (PSA), Food Safety Preventive Controls Alliance (FSPCA), and Sprout Safety Alliance (SSA) have developed training programs to help domestic and foreign food businesses—including small and very small farms and facilities—understand the requirements of the preventive controls regulations, FSVP, the Intentional Adulteration rule, and the Produce Safety rule. The Alliances are composed of representatives from the government, including FDA, USDA, and state regulatory agencies, the food industry, and academia.

The Alliances are working to ensure that training opportunities available to international food businesses are consistent with those being provided domestically. FSPCA—working with PSA, as well as representatives of importers and foreign governments, and others—has established an International Subcommittee to address the training, education, and technical assistance needs of global stakeholders.

To further address the training needs of the global food industry, FDA and the University of Maryland established through a cooperative agreement the Joint Institute for Food Safety and Applied Nutrition (JIFSAN) to support FDA's mission through the delivery of food safety training programs throughout the world. Among other things, JIFSAN oversees the implementation of international education, outreach, and training, delivers international trainings, and establishes relationships with organizations that may provide technical assistance to the foreign farming community. JIFSAN is currently engaged in training efforts on FSMA to international audiences.

To meet the specific training and technical assistance needs of local food and tribal producers, FDA established relationships with and provided financial support to groups that can best meet the training and technical assistance needs of these populations. One such group is tasked with bringing training to tribal producers and food businesses to fulfill the requirements of FSMA, while another group is tasked with providing training, education, and outreach to local producers and processors to enhance the fundamental knowledge of food safety and to help these local producers and processors comply with applicable FSMA regulations.

FDA recognizes the importance of engaging with our state partners on FSMA implementation, especially in the implementation of the Produce Safety rule. One of the resources now available to farmers is the On-Farm Readiness Review (OFRR) program. The National Association of State Departments of Agriculture (NASDA) created this program in collaboration with FDA. On-Farm Readiness Reviews are voluntary and provide farmers real-time feedback on their current operations and facilities before inspections begin in 2019. Working together, the aim is to improve the safety of the food supply.

Additionally, FDA provides funding to states, through a series of state produce cooperative agreements, to establish produce regulatory programs that include inspections, training, outreach, and technical assistance elements. FDA is also providing training to state regulators on produce

safety and preventive controls inspections and works with our state partners to roll out inspection programs for the preventive controls rules.

2. 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 2,000 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 postmarketing setting.

3. Comprehensive Tobacco Framework

The Committee commends the FDA for its 2017 comprehensive plan for tobacco and nicotine regulation to protect public health and create more predictability in tobacco regulation via the consideration of reduced-risk products. FDA must balance the needs of current adult smokers with the risks of attracting new youth to the marketplace. As FDA moves forward, the Committee directs the agency to consider foundational regulations and guidance for its new rulemakings, including for the Substantial Equivalence (SE) and Pre-market Tobacco Application (PMTA) pathways. These rulemakings should reflect a minimum of 24 months for compliance and additional flexibility and assistance for small tobacco product manufacturers. Clear definitions of terms and requirements for submission to FDA, including those for same characteristics and questions related to public health, will help to provide certainty and limit excessive speculation in

the process. A foundational approach to rulemaking and guidance should also rely on product standards, reference products for the SE pathway, performance standards for FDA in certifying reports and applications, and the acceptance of identical specifications in SE reports. In providing transparency, FDA should consider the quarterly release of Center for Tobacco Products reviewer guides. Finally, FDA should consider the expedited or privileged review of quantity and packaging changes that do not affect the core characteristics of products in the PMTA process.

FDA Response:
FDA's comprehensive plan for tobacco and nicotine regulation will serve as a multi-year roadmap to better protect kids and significantly reduce tobacco-related disease and death. As part of this comprehensive plan, FDA announced that it will issue foundational rules to make the product review process more efficient, predictable, and transparent for manufacturers, while also advancing the agency's public health mission. Among other things, FDA intends to issue proposed regulations outlining what information the agency expects to be included in Premarket Tobacco Product Applications (PMTAs) and Substantial Equivalence Reports (SE Reports). The first of these foundational rules for SE Reports is currently in the interdepartmental review process at the Office of Management and Budget. FDA also intends to issue product standards on electronic nicotine delivery systems (ENDS) and testing standards for batteries and battery management systems in ENDS. Additional information about FDA's regulatory activities under development can be found in the latest edition of the Unified Agenda, which is published twice a year in the spring and fall. When each proposed rule is issued, the Agency will solicit comments from the public on all aspects of the rule and will take all of the comments into consideration before issuing a final rule. In addition, FDA intends to provide further information on its thinking with respect to premarket review through guidance documents, as appropriate, such as on considerations relevant to ENDS and the PMTA pathway.

On October 22 and 23, 2018, FDA held a public meeting to improve public understanding and seek feedback on the policies and processes for the submission and review of tobacco product marketing applications, including the general scientific principles relevant to various application pathways, in order to assist applicants considering submitting marketing applications for tobacco products.

Additionally, FDA intends to continue providing web updates with information around decisions and the basis for those decisions. These updates are intended to provide transparency around the timing and review of submissions, including submissions that may only need a limited amount of information (e.g., changes to quantity or packaging). The web updates also provide information on certain deficient applications and how those deficiencies could be addressed to obtain a marketing order. On August 14, 2018, FDA announced that it will proactively provide applicants certain reviews to facilitate understanding of a provisional Not Substantially Equivalent (NSE) decision. Applicants are no longer required to file a Freedom of Information Act request to obtain these documents following a decision.

4. Dairy Labeling Requirements

The Committee is aware of the concerns with labeling certain foods and beverages as a dairy product when the product is plant-based rather than derived from animals. The Committee directs the FDA to develop a standard of identity for dairy products based upon the dairy product terms

described in parts 131, 133, and 135 of subchapter B of chapter I of title 21, Code of Federal Regulations within 180 days from the date of enactment of this Act. The FDA should issue guidance to industry on how to implement the standard of identity, including how this standard will be enforced.

FDA Response:
FDA takes seriously its responsibilities under federal law to protect consumers from misbranded food and understands the Committee's concern regarding plant-based products marketed with names that include the names of standardized dairy foods, e.g., "milk."

Under FDA's Nutrition Innovation Strategy, the Agency is undertaking efforts to modernize the framework for standards of identity. In addition to these efforts, the agency is considering the labeling of plant-based dairy alternatives.

To help the FDA examine the labeling of plant-based dairy alternatives, on September 27, 2018, FDA issued a request for comments and data from stakeholders about consumer awareness, understanding, and perceptions, including nutritional considerations, of these products when labeled with names that include the names of dairy foods. The docket closed on January 28, 2019, and the comments we receive will help inform the development of draft guidance to provide greater clarity on labeling of plant-based dairy alternatives.

5. Food Date Labeling

The Committee recognizes that the lack of food date labeling standardization has resulted in significant consumer confusion. Because food manufacturers use a variety of food date labeling phrases, such as ''freshest by'' or ''use by,'' consumers frequently throw out food that is wholesome and safe, which contributes to the country's food waste problem. The Committee encourages FDA and USDA to provide outreach and guidance to food manufacturers and retailers on food date labeling.

FDA Response:
FDA is committed to improving consumer knowledge about the safety and quality of the food they purchase, including how to understand the handling information and date labels that appear on packaged food.

FDA is responsible for promoting and protecting the public's health by ensuring that the nation's food supply is safe, sanitary, wholesome, and honestly labeled. No federal law or regulation requires date labels, such as expiration dates and use-by dates, on food products, except for infant formula. Any date labels that are used, however, must be truthful and not misleading.

FDA is aware of ongoing efforts by government agencies, industry groups, non-governmental organizations, academia, and others to promote standardized date label phrases and to educate consumers about the meaning of quality-based dates. FDA has engaged in these discussions and continues to enhance its consumer messages related to the meaning of voluntary date labels.

FDA is also working to address the broader problem of food waste through the *Winning on Reducing Food Waste Initiative,* which was recently established through an intergovernmental agreement signed between FDA, the Environmental Protection Agency (EPA), and the U.S. Department of Agriculture (USDA). The agreement is aimed at improving coordination and communication across federal agencies attempting to better educate Americans on the impacts

and importance of reducing food loss and waste. In August 2018, FDA appointed a representative to an interagency discussion group on food waste that is coordinated by USDA and includes representatives from EPA and the National Oceanic and Atmospheric Administration. The group meets every three weeks to consider ways the agencies can work together on food loss and waste initiatives.

As these efforts continue, FDA will consider whether guidance on food date labeling might be appropriate for food manufacturers.

6. Naloxone to Treat Over-usage of Opioids

United States public health agencies have appropriately highlighted the risk of overdose from doses of opioids greater than 90 morphine milligram equivalents (MME) per day. Also concerning are the hundreds of millions of prescriptions each year of immediate release (IR) lower MME opioids such as hydrocodone and oxycodone. These opioids are commonly associated with abuse and are a common pathway to addiction and also present a risk of overdose. Some states have begun to limit the prescribing of these IR opioids. An additional consideration might be to assess the benefit of co-prescribing naloxone with IR and extended release (ER) opioids. Prescribers including dentists and other primary care providers have an opportunity to become more attuned to the risks of all opioids through the consideration of co-prescribing naloxone with each opioid prescription. The Committee requests the FDA develop a strategy to test this hypothesis and assess the benefit for enacting such a policy as a national strategy.

FDA Response:
FDA remains committed to fighting the opioid crisis and will continue to advance using a multipronged strategy. FDA is focusing on four broad areas to help address the opioid crisis: 1) decreasing exposure and preventing new addiction; 2) supporting the treatment of those with opioid use disorder; 3) fostering the development of novel pain treatment therapies; and 4) improving enforcement and assessing benefit-risk. To advance these goals, FDA is supporting cutting-edge research to facilitate the evaluation of abuse-deterrent formulations, alternatives to opioids for pain, and the development of medications that can help patients with addiction recover as well as overdose reversal drugs, such as naloxone.

FDA continues efforts to make naloxone more broadly available. Naloxone is currently a prescription drug nationwide. FDA has reached out to, and met with, sponsors of naloxone products to offer advice and assistance on expediting development of a nonprescription (OTC) naloxone drug product. Prescription drug products, including prescription naloxone, require the supervision of a healthcare professional for safe and effective use. OTC drug products, on the other hand, must be able to be used safely and effectively without the supervision of a healthcare professional. The information necessary for safe and effective use of OTC drug products is conveyed to consumers by the Drug Facts labeling (DFL). Typically, DFLs are developed and scientifically tested by drug manufacturers prior to submission of an application for approval of an OTC drug to show that consumers can follow the DFL to understand how to use the product without the help of a healthcare professional. In the case of naloxone, FDA has taken the

unprecedented step of developing a model DFL that is intended to convey all the important information a consumer would need to use naloxone effectively and safely in an emergency overdose situation. After developing the model DFL, FDA awarded a contract to an experienced consumer research firm, for rigorous scientific testing of consumer comprehension of the DFL. The study has concluded and an independent FDA review team is currently analyzing the data. Once analysis is complete, the results of the study will be made publicly available for use by manufacturers of naloxone products who wish to submit an application to FDA for an OTC naloxone product.

In addition, on December 17-18, 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.

7. Olive Oil Standards of Identity

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 pomace oils.

The Committee is particularly concerned with the number of different oil 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 extra virgin olive oil representatives and olive oil representatives in developing a science-based Standard of Identity for extra virgin olive oil and olive oil, respectively, 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.

8. Performance Measures

The Committee directs FDA to comply with title 31 of the United States Code, including the development of their organizational priority goals and outcomes such as performance outcome measures, output measures, efficiency measures, and customer service measures.

FDA Response:
FDA will comply with Title 31 of the United States Code.

9. Sunscreen Ingredients

The Committee remains significantly concerned that the FDA has not approved a new over-the-counter (OTC) sunscreen ingredient since the 1990s despite increased skin cancer rates in the United States, the Surgeon General's 2014 Call to Action to Prevent Skin Cancer, unanimous passage of the Sunscreen Innovation Act (SIA) in Congress and having a number of ingredients pending approval for more than 15 years. The Committee directs the FDA to continue to work with sponsors to reach a path forward on a testing regimen for sunscreen ingredients that is consistent with current scientific standards, has a proven track record with sunscreen ingredients, and appropriately balances the benefit of additional skin cancer prevention tools.

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*, 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 the sunscreen containing the active ingredient would be Generally Recognized as Safe and Effective (GRASE).[121] The Agency has also 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. Although not required to do so by the SIA,

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

FDA continues to meet with sponsors upon request to discuss data development.[122] In May 2018, FDA published a draft guidance that, when finalized, will provide manufacturers with recommendations for how to conduct a MUsT (maximal usage trial) for topically applied active ingredients being considered for inclusion in an OTC drug monograph, including sunscreen active ingredients.[123] To date, the Agency has not received any additional data from manufacturers for any of the pending sunscreen ingredients that were the subject of SIA-required proposed sunscreen orders issued in 2015.

To date, FDA has met all statutorily mandated SIA deadlines and remains committed to achieving that goal in the future. The FDA is working to finalize OTC monograph regulations for sunscreens by November 26, 2019, as required by the SIA.

[122] Regulations.gov (November 15, 2017). Retrieved November 15, 2017, from www.regulations.gov/document?D=FDA-2005-N-0453-0051.

[123] Guidance for Industry. Maximal Usage Trials for Topical Active Ingredients Being Considered for Inclusion in an Over-The-Counter Monograph: Study Elements and Considerations.
https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM608356.pdf