

HOUSE APPROPRIATIONS COMMITTEES SIGNIFICANT ITEMS

HOUSE COMMITTEE REPORT (114-531)

1. Animal Drug Compounding

The Committee is concerned that the FDA has proposed draft guidance for industry (#230) for animal drug compounding that applies Sections 503A and 503B of the FDCA to animal health even though these provisions were written in regard to compounding of human drugs. The Committee is concerned that this will result in confusion in the industry and may result in a misallocation of the resources Congress makes available to the FDA to oversee compounding activities. The Committee expects that any final guidance on animal drug compounding will reference statutory provisions that specifically relate to veterinary practices.

FDA Response:

FDA issued the draft Guidance for Industry (#230), “Compounding Animal Drugs from Bulk Drug Substances,” to provide clarity regarding the conditions under which FDA generally would not intend to take action against state-licensed pharmacies, licensed veterinarians, and outsourcing facilities for compounding animal drugs from bulk drug substances. Animal drugs compounded from bulk drug substances do not have legal marketing status under the Federal Food, Drug, and Cosmetic Act (FD&C Act); however, FDA recognizes that such drugs may be a necessary and appropriate treatment option for animals in certain circumstances. Thus, this draft Guidance provides FDA’s thinking on our enforcement discretion in this area.

In the draft guidance, FDA is not proposing to apply sections 503A or 503B of the FD&C Act to the compounding of animal drugs from bulk drug substances. However, some of the conditions proposed in the draft guidance appear similar to conditions in section 503B, where appropriate. FDA proposed this approach because many of the concepts embodied in sections 503A and 503B may be appropriate for animal drugs, as well as for human drugs. Additionally, many compounders who compound human drugs also compound animal drugs and are already familiar with this framework and can readily implement it. The approach taken in the draft guidance reflects FDA’s intent to strike the proper balance between the need to provide access to compounded drugs, when necessary, and the need to preserve the integrity of the animal drug approval process, which provides assurances that drugs are safe and effective, properly manufactured, and appropriately labeled.

In regard to finalizing the draft guidance, FDA received more than 150 comments on the draft guidance. FDA will carefully consider these comments and other information received before finalizing the draft guidance.

2. Antibiotics

The Committee urges the FDA to work to foster the development of new antibiotics by supporting greater collaboration between industry and the FDA around adaptive clinical trials and labeling changes. The President’s Council of Advisors on Science and Technology has

recommended this proposal to help support the type of robust drug development that will be needed to ensure patients are protected from bacterial resistance.

FDA Response:

FDA considers mitigation and prevention of antibiotic resistance a top priority. FDA will continue to collaborate with experts from academia, the pharmaceutical industry, professional societies, patient advocacy groups, and other Public Health Service agencies to find solutions to scientific challenges in the development of new antibacterial drugs.

A draft Guidance for Industry document on possible streamlined drug development pathways for drugs intended for the treatment of serious bacterial diseases in patients who have an unmet medical need has been published that includes recommendations for clinical trial designs and labeling. The Limited Population Pathway for Antibacterial and Antifungal Drugs (LPAD) established as part of the 21st Century Cures Act allows FDA, at an applicant's request, to approve an antibacterial or antifungal drug as a limited population drug. Some antibacterial drugs that are candidates for a streamlined development program may also be candidates for LPAD. In certain circumstances, LPAD will allow FDA to conclude that the benefits of a drug outweigh its risks in a particular limited population, despite greater uncertainty. FDA is developing draft guidance describing the criteria, processes, and other general considerations for demonstrating the safety and effectiveness of limited population drugs.

Cooperation between FDA and industry, along with our partners in other Public Health Service agencies, could facilitate advancements in the field. These efforts should help to facilitate the development of new antibacterial drugs to address patient needs.

3. Biological Products

The Committee commends the FDA for issuing draft guidance to address the mixing, diluting, or repackaging of biological products outside the scope of an approved biologics license application. The Committee urges the FDA to finalize the guidance without delay following the public comment period and continues to emphasize the need for close FDA inspection and supervision of large-scale compounding and repackaging of sterile injectable drugs and biological products, particularly products that are administered into areas of the human body where there is tempered immunity, such as the eye or spinal column, to ensure that they are processed in keeping with current good manufacturing practice for sterile products, in particular 21 CFR 200.50 regarding ophthalmic preparations.

FDA Response:

FDA shares the Committee's concern about the public health risks associated with improper manipulation of sterile, injectable drug products, including biological products. FDA has been working to balance minimizing public health risks with ensuring that patients have access to medicines appropriate for their health needs. In January 2017, FDA issued a revised draft guidance concerning mixing, diluting, and repackaging biological products by state-licensed pharmacies, federal facilities, physicians, and outsourcing facilities. The revised draft guidance, published for public comment, includes changes to address comments that FDA received on the

initial draft guidance. The comment period on the revised draft guidance closed on March 14, 2017, and FDA received 11 comments. FDA intends to review the comments and finalize the guidance document as quickly as possible.

4. Biosimilars

The Committee recognizes that biosimilars offer an important opportunity for expanding the market and reducing costs for patients. The Committee urges the FDA to partner with external stakeholders including patient organizations on educating patients and professionals about biosimilars, with a focus on populations for which approved biosimilars are indicated.

FDA Response:

FDA remains committed to working with stakeholders, including drug manufacturers, prescribers, pharmacies, hospitals and health systems, informatics providers, and patient groups on this important issue.

5. Blood Donor Policies

The Committee commends the FDA on updating their blood donor policy in the December 2015 Guidance to Industry from a lifetime ban to a one year deferral, however it continues to encourage a permanent policy change based on scientifically supported risk factors and not time passed. The Committee remains concerned that certain questions on the FDA blood donor questionnaire are outdated and discriminatory. This questionnaire should not ask about sexual orientation, rather it should assess risk factors that might expose a potential blood donor to blood-borne illness. The Committee encourages FDA to find an adequate replacement question for the blood donor questionnaire that is cognitively appropriate and will maintain a safe donor pool without discrimination.

FDA Response:

FDA is committed to reevaluating and updating its blood donor deferral policies to reduce the risk of HIV transmission as new scientific data become available. FDA changed its recommendations from an indefinite deferral for men who have sex with men (MSM) to a 12-month deferral from the last sexual contact as described in the December 2015 guidance. This change has been implemented widely by blood collection establishments since that time. In July 2016, FDA established a public docket for comment on the Agency's blood donor deferral recommendations for reducing the risk of HIV transmission by blood and blood products. Specifically, with regard to the 12-month deferral for MSM, FDA invited the submission of scientific evidence on the feasibility of moving from the existing time-based deferrals related to risk behaviors to alternate options, including the use of individual risk assessments. To date, 670 comments were received (many against further policy change), a number of comments provided recommendations, some of which were supported by scientific evidence.

Over the next years, FDA plans to study the feasibility, effectiveness, and operational impact of alternative donor history questionnaires. These alternatives would include individual risk assessment questionnaires that do not ask about sexual orientation.

Additionally, FDA has launched initiatives to facilitate new “real time” monitoring of markers of transmissible infectious diseases and related risk factors in donors of blood components. In September 2016, FDA in collaboration with the National Heart, Lung and Blood Institute, and the Department of Health and Human Services (HHS) Office of the Assistant Secretary for Health, established the Transfusion-Transmissible Infections Monitoring System (TTIMS). This system should provide invaluable data for estimating the incidence and prevalence of HIV, hepatitis B virus, and hepatitis C virus infection in blood donors. TTIMS is actively assessing transfusion-transmitted infection markers, behavioral risk factors for positive donors, and other epidemiologic variables among voluntary U.S. blood donors that may be useful to assess changes in the donor base including the impact of the change made to the MSM deferral.

6. Centers of Excellence

The Committee is encouraged by the ongoing research and collaboration underway at the Centers of Excellence in Regulatory Science and Innovation (CERSI) program. The Committee believes that these programs will help the agency improve public health, address scientific challenges presented by revolutions in medical product development, and improve food safety and quality. The Committee commends the agency for launching this program in 2011 and expanding it in 2014. For this reason, the Committee believes that the agency should continue to invest in the existing four locations in the CERSI network at their original funding level to ensure their efficacy and to capitalize on existing studies.

FDA Response:

FDA appreciates the recognition of the importance of the CERSIs, their contributions to regulatory science, and identification of support for them. FDA plans to support four CERSIs under the new grant awards that were made in FY 2016. Three of these are existing CERSIs and one is new.

7. Compassionate Use

The Committee is aware of GAO’s current plans to conduct a review of the FDA’s work with patient stakeholder groups as it relates to Expanded Access or Compassionate Use of human drugs. The Committee encourages the FDA to work with GAO in order to provide them with all the necessary information they need to complete their review of the program.

FDA Response:

FDA is committed to working with GAO and providing the necessary information they need to complete their review.

8. Continued FDA Approval of Drug Safety Labeling

The Committee is deeply concerned with the FDA's failure to resolve issues with and finalize its proposed rule entitled "Supplemental Applications Proposing Labeling Changes for Approved Drugs and Biological Products." The proposed rule, as currently drafted, has the potential to threaten public health and create unprecedented patient and provider confusion by allowing multiple versions of safety labeling for the same bioequivalent product. The Committee urges the FDA to establish in the final rule a system where safety information in prescription drug labeling in a multisource environment (i.e., when there is both an innovator and a generic manufacturer or more than one generic manufacturer) is always FDA-approved, grounded in scientific evidence, and presents no opportunity for mismatched safety information between the innovator and generic versions of a drug. The FDA should be the final decision maker regarding whether a manufacturer should change its labeling in a multisource environment. The FDA is the only entity that possesses all of the clinical trial, safety, and post-marketing data submitted by all manufacturers. Only the agency has all of the necessary tools to make an informed decision when it comes to making safety labeling changes, and, as a result, consistent with the FDA's responsibility to approve drug applications and labeling prior to marketing, only the FDA should determine whether a safety labeling change should occur.

FDA Response:

The proposed rule was intended to improve the communication of important drug safety information to healthcare professionals and patients. FDA has received a great deal of public input from stakeholders during the comment period on the proposed rule regarding the best way to accomplish this important public health objective.

FDA is carefully considering comments submitted to the public docket established for the proposed rule from a diverse group of stakeholders including: consumers and consumer groups, academia (including economists), health care associations, drug and pharmacy associations, brand and generic drug companies, law firms, state governments, and Congress, including comments proposing alternative approaches to communicating newly acquired safety-related information in a multi-source environment (see FDA-2013-N-0500). These comments include a summary of FDA's meeting with the Generic Pharmaceutical Association (GPhA) on September 8, 2014, to listen to their comments and views regarding the proposed rule.

In addition, FDA held a public meeting at which any stakeholder had the opportunity to present or comment on the proposed rule, or on any alternative proposals intended to improve communication of important, newly acquired drug safety information to healthcare professionals and the public. In the February 18, 2015, notice announcing the public meeting, FDA reopened the docket for the proposed rule until April 27, 2015, to allow the submissions of written comments concerning proposals advanced during the public meeting. FDA will determine next steps based on our analysis of comments on the proposed rule and additional information submitted as part of the public meeting.

9. Crop Biotechnology & Biotech Ingredients

Plants, food, and food ingredients developed using genetic engineering were introduced into the U.S. food supply in the 1990s. Public and private sector scientists knowledgeable in genetic engineering, toxicology, chemistry, nutrition, and other scientific areas have carefully evaluated

and assessed the safety of these products and have determined that such products are safe for human and animal consumption. The Committee provides a total of \$3,000,000 for the FDA to coordinate with the U.S. Department of Agriculture (USDA) to provide education and outreach to the public on the safety and benefits of crop biotechnology and food and animal feed ingredients derived from biotechnology. The Committee expects this educational information to be posted on both agency websites and through other social media and communications platforms within 60 days of enactment of this Act.

FDA Response:

FDA continues to work with USDA and the U.S. Environmental Protection Agency (EPA), under the [Coordinated Framework for the Regulation of Biotechnology](#), to promote public confidence in the oversight and development of safe biotechnology products. In an ongoing effort to [modernize the regulatory system for biotechnology products](#), FDA (along with EPA and USDA) is reviewing existing communication tools and, as appropriate, may revise existing or develop new user-friendly sources of regulatory information for product developers and the general public.

FDA's communications materials discuss the Agency's regulatory role in ensuring that foods from genetically engineered (GE) plants meet the same food safety requirements as foods derived from traditionally bred plants. The materials encourage GE plant developers to participate in FDA's voluntary Plant Biotechnology Consultation Program to foster collaboration and transparency and enhance regulatory compliance. FDA and industry coordination and cooperation increases public trust in the safety of foods from GE plants – and confidence in regulatory and industry communications about food safety evaluations.

FDA does not address potential agricultural, environmental (e.g., pest control, weed control, land use, irrigation, yield, etc.) or humanitarian benefits which are beyond the scope of its mandate or expertise. To help maintain public confidence in FDA's role in conducting food safety reviews, FDA believes it is more appropriate for other agencies to take the lead in conveying messages regarding the benefits of biotechnology within their purview and expertise. Additionally, to conduct an educational campaign of the magnitude envisioned in the House report would require significantly more than 60 days to produce, pilot test, and disseminate the necessary consumer outreach materials.

If provided an additional \$3,000,000 in budget authority above FY 2016 funding levels to carry out education and outreach on crop biotechnology oversight, FDA would do so in cooperation with partners such as USDA and EPA. Funds likely would be provided to an outside contractor to assist in the education campaign. Wherever possible, FDA would leverage existing subject matter experts to support this effort. However, without additional funding in FY 2017, this requirement will impose a significant burden on existing staff and will divert resources away from other important biotechnology initiatives (e.g., consideration of new biotechnology methods and the safety of foods derived from them), as well as other education and outreach efforts.

10. Date Labels on Food

The Committee is concerned by the amount of food waste resulting from consumer confusion around date labels on food. The Committee notes that there is currently no federal uniform

system for food date labels, which are currently determined by the food company to indicate quality rather than the safety of the food. The Committee urges FDA to study current and potential date labeling language and formats to determine what language and/or format is most effective in reducing consumer confusion and communicate such voluntary options to food producers.

FDA Response:

A principle of U.S. food law is that foods in U.S. commerce must be fit for consumption. The FD&C Act places a legal duty on manufacturers, processors, and distributors to ensure that the foods they market to consumers are safe and comply with all legal requirements. A "best by," "use by," or expiration date does not relieve a firm from this obligation. A product that is dangerous to consumers would be subject to potential action by FDA to remove it from commerce regardless of any date printed on a label. With the exception of infant formula, the laws and regulations enforced by FDA leave to manufacturers the decision whether to place and what criteria to use in placing "expired by," "use by," or "best before" dates on food products; however, FDA regulations that prohibit manufacturers from labeling food in a manner that is misleading or deceptive apply to the use of such statements.

Parties seeking solutions to the problem of food waste in the United States often point to the absence of a national uniform system for date labeling for packaged foods as a key factor that contributes to food waste. Advocates for more uniform date labels cite data suggesting that consumers mistakenly believe that these dates are indicators of safety, and therefore report throwing food away once the date passes, due to fear of safety risks. In recent years, a National Food Waste Reduction Goal has served as a mechanism for bringing greater attention to food waste. FDA has been working to explore ways to reduce food waste while not compromising the safety of the U.S. food supply as part of this effort, and has engaged with the designated lead federal agencies (USDA and EPA) and various trade associations and non-governmental organizations.

11. Drug Compounding

The Committee believes patient access to the right drug at the right time is of utmost importance. In instances where a commercially manufactured drug is not appropriate for a patient for a specific reason, a compounded drug may be the difference between life and death. Since passage of the Drug Quality and Security Act (DQSA) of 2013, the Committee has had concerns that the FDA interpreted provisions of Section 503A of the FDCA in a manner that might jeopardize the availability of compounded medications for "office use." The practice of "office use" occurs when a compounder will compound a batch of drugs in anticipation of receiving patient-specific prescriptions at a later time. It may also be the case of a doctor in his or her office maintaining compounded drugs on site because it is unsafe or impractical to issue a traditional prescription. This practice is authorized in the vast majority of states and was intended to be allowable under DQSA. The Committee is aware that on April 15, 2016, FDA released a new Draft Guidance on the issue of "office-use" compounding. The Committee directs the FDA to issue a Final Guidance that provides for "office-use" compounding of drugs, in appropriate circumstances as well as including drugs compounded in anticipation of a prescription for an identified individual patient. Such "anticipatory" compounded drugs must be based on the history of previous valid

compound prescription orders, and on an established history between the prescriber and the patient and the compounder.

FDA Response:

FDA shares the Committee’s concern about protecting access to compounded drugs for “office use.” FDA is committed to implementing policies in a way that preserves access to compounded drugs, while protecting patients from poor quality compounded drugs that could cause death or serious injury. The policies set forth in FDA guidance documents implement the statutory provisions that provide for compounding and distribution of drugs for office use by outsourcing facilities under section 503B of the FD&C Act and anticipatory compounding by compounders under section 503A of the FD&C Act.

As you noted, in April 2016, FDA issued draft guidance for public comment titled *Prescription Requirement Under Section 503A of the Federal Food, Drug, and Cosmetic Act*. FDA issued the final guidance in December 2016. As discussed in this guidance, compounding under section 503A of the FD&C Act must occur either after the receipt of a prescription for an identified individual patient (section 503A(a)(1)), or in limited quantities before the receipt of a prescription for an identified individual patient (section 503A(a)(2)). Section 503A does not provide for the distribution of a compounded drug without the compounder first receiving a prescription for an identified individual patient (e.g., for office use).

In contrast, entities that are registered with FDA as outsourcing facilities under section 503B of the FD&C Act can distribute compounded drugs for office use without receiving patient-specific prescriptions (section 503B(d)(4)(C)). FDA is not aware of specific drug products needed for office use that are not supplied by outsourcing facilities.

The prescription requirement in section 503A of the FD&C Act is critical to protecting patients. Although compounded drugs can serve an important need, they pose a higher risk to patients than FDA-approved drugs. Compounded drug products are not FDA-approved, which means they have not undergone FDA premarket review for safety, effectiveness and quality. In addition, although drugs compounded by licensed pharmacists and licensed physicians in accordance with section 503A are subject to certain requirements of the FD&C Act, such as the prohibition on preparing drugs under insanitary conditions, they are not subject to manufacture according to CGMP requirements. Because such compounders generally do not register their compounding facilities with FDA and are not under routine FDA surveillance, FDA is often not aware of potential problems with their compounded drug products or compounding practices unless it receives a complaint such as a report of a serious adverse event or visible contamination. When FDA has conducted inspections of state-licensed pharmacies because of serious adverse events or contamination, we have observed serious deficiencies in drug production practices and conditions that could put patients at risk.

For these reasons, patients should only receive compounded drugs if their needs cannot be met by an FDA-approved drug product. The prescription requirement is critical to ensure that compounding by state-licensed pharmacies and physicians under section 503A is based on individual patient need, to differentiate such compounding from conventional manufacturing, and to differentiate compounding by pharmacists and physicians who are primarily subject to state regulation from compounding by outsourcing facilities, which are primarily subject to FDA regulation. Compounding for office stock by 503A facilities would undermine the incentive for

compounders to become outsourcing facilities, a critical measure that Congress put in place in the DQSA to prevent another outbreak on the scale of the 2012 fungal meningitis outbreak, which resulted in over 60 deaths and 750 cases of infection.

12. Drug Compounding Inspections

The Committee understands that the FDA is interpreting provisions of Section 503A of the FDCA to inspect state licensed compounding pharmacies under current Good Manufacturing Practices (cGMPs) instead of under the standards contained in the United States Pharmacopeial Convention (USP) for sterile and non-sterile pharmaceutical compounding or other applicable pharmacy inspection standards adopted by state law or regulation. The Committee reminds the FDA that compounding pharmacies are not drug manufacturers, but rather, are state licensed and regulated health care providers that are inspected by state boards of pharmacy pursuant to state laws and regulations that establish sterility and other standards for the pharmacies operating within their states. Compounding pharmacies are more appropriately inspected using USP standards or other pharmacy inspection standards adopted by state law or regulation in the state in which a pharmacy is licensed.

FDA Response:

After the 2012 fungal meningitis outbreak, and until August 2016, FDA investigators had been listing on Forms FDA-483 inspectional observations relating to deviations from drug production practices that could lead to quality problems without regard to whether the observations related to current good manufacturing practice (CGMP) requirements deficiencies or other deficiencies.

Only after the inspection did FDA determine whether the state-licensed pharmacies failed to meet the conditions of section 503A of the FD&C Act, and, as a result, the drugs compounded in their facilities were ineligible for the exemption from CGMP requirements in section 503A. This practice led to the perception that FDA was imposing CGMP requirements on state-licensed pharmacies even if they met the conditions of section 503A.

In response to stakeholder input, FDA changed its practice. As of August 2016, FDA only includes on the Form FDA-483 observations related solely to CGMP requirements if, based on the FDA investigator's preliminary assessment, the compounder produces drugs that are not eligible for the exemptions under section 503A. This change in practice has reduced the number of state-licensed pharmacies receiving Forms FDA-483 listing observations related solely to CGMP requirements. Yet, FDA continues to issue Forms FDA-483 listing observations related solely to CGMP requirements because FDA investigators find that the majority of state-licensed pharmacies they inspect are not meeting the conditions of section 503A and, therefore, preliminarily assess that the pharmacies' drug products are subject to CGMP requirements.

Furthermore, although drugs compounded by pharmacies that meet the conditions of section 503A qualify for exemptions from three provisions of the FD&C Act, including CGMP requirements, they remain subject to all other applicable provisions of the FD&C Act related to the production of drugs. For example, drugs compounded by pharmacies operating under section 503A must not be prepared, packed, or held under insanitary conditions whereby the drug may have been contaminated by filth, or whereby it may have been rendered injurious to health. Section 501(a)(2)(A).

When FDA finds that a pharmacy compounds drugs in accordance with section 503A and does not violate other applicable Federal laws, FDA generally defers regulatory oversight of the pharmacy to the state, but when a pharmacy fails to produce drugs in accordance with section 503A or violates other Federal laws, such as preparing, packing, or holding drugs under insanitary conditions, FDA may pursue regulatory action.

With respect to the Committee's statement that "compounding pharmacies are more appropriately inspected using USP standards or other pharmacy inspection standards adopted by state law or regulation in the state in which a pharmacy is licensed," FDA inspects compounding facilities for compliance with applicable Federal requirements, not "inspection standards adopted by state law or regulation." FDA cannot tailor each inspection to the unique standards of 50 different states, and a pharmacy may be licensed in many states, each with different requirements. For example, some states require compliance with USP Chapters 795 and 797, but many do not.

FDA collaborates with its state partners on regulation of compounding. However, we also have an obligation to take our own action to protect the American public from adulterated, misbranded, and/or unapproved new drugs produced by compounding facilities in violation of Federal law. If we do not, it will become more likely that another outbreak could occur like the 2012 fungal meningitis outbreak, which resulted in over 60 deaths and over 750 cases of infection.

13. Drug Compounding of Allergen Extracts

The Committee is concerned that proposed changes to general chapter 797 of the USP contradicts the legislative intent of Section 503A of DQSA regarding the practice of "office-use" compounding of allergen extracts. The FDA recognizes USP general chapter 797 as federal policy on the practice of drug compounding. The Committee is concerned that the proposed changes to USP general chapter 797 would be inconsistent with its legislative intent of Section 503A and with the agency's own previous positions on the practice of office-use compounding of allergen extracts. It is the sense of the committee that the practice of office-use compounding of allergen extracts by physicians is proven to be both safe and effective for the diagnosis and treatment of allergic conditions. The Committee suggests that the USP work with organizations from the physician and patient communities that represent physicians who regularly engage in office-use compounding of allergen extracts or patients who benefit from such compounding of allergen extracts, to ensure that any changes to USP general chapter 797 regarding office-use compounding of allergen extracts are reflective of the clear legislative intent of Section 503A of the DQSA.

FDA Response:

At the outset, the Committee should be aware that the USP is an independent, non-governmental standard-setting organization. Representatives of FDA serve as liaisons to certain USP expert committees to provide recommendations and guidance on scientific and public health matters, but FDA liaisons are not voting members of USP expert committees and do not control the standards that the USP establishes.

Section 503A of the FD&C Act does not apply to biological products, including allergenic extracts that are subject to licensure under section 351 of the PHS Act. Section 503A describes the conditions that must be met for certain compounded drug products to qualify for exemptions from three provisions of the FD&C Act, including new drug approval requirements in section 505. Although section 503A provides an exemption for certain compounded drugs from the requirement to obtain premarket approval under section 505 of the FD&C Act, it does not provide an exemption from the requirement to obtain premarket approval under section 351 of the PHS Act. Manufacturers of biological products, including allergenic extracts, are required to obtain an approved license under section 351 of the PHS Act. Because section 503A does not provide an exemption from the licensure requirement under section 351 of the PHS Act, for purposes of section 503A, the term *drug* does not include any biological product that is subject to licensure under section 351 of the PHS Act. Accordingly, such biological products are not eligible for the exemptions for compounded drugs in section 503A of the FD&C Act.

Combinations of licensed allergenic extracts as prescription sets for subcutaneous treatment of individual patients who have allergies have not been reviewed for safety, purity, and potency and licensed by FDA. Nevertheless, FDA recognizes the importance of preserving patient access to such products when they meet appropriate quality standards to prevent patient harm. In January 2017, FDA published for public comment a revised draft guidance document titled, “Mixing, Diluting, or Repackaging Biological Products Outside the Scope of an Approved Biologics License Application.” Among other things, this revised draft guidance will, when finalized, describe FDA’s current thinking regarding State-licensed pharmacies, Federal facilities, outsourcing facilities, and physicians that prepare prescription sets of allergenic extracts. The revised draft guidance states, in part, that FDA does not intend to take action for violations of section 351 of the PHS Act or sections 502(f)(1), 582, or 501(a)(2)(B) of the FD&C Act if prescription sets are prepared by a State-licensed pharmacy, Federal facility, or physician in accordance with certain conditions. One of these conditions is that the prescription set be prepared in accordance with USP Chapter 797, with the exception of the beyond use date, which is addressed separately in the guidance.

The revised draft guidance refers to the current USP Chapter 797 (USP 39-NF 34 (2016)), and not to USP’s proposed revision. The revised draft guidance further explains that FDA intends to consider whether to update its guidance document to refer to the revised chapter once USP issues a final revision to Chapter 797. FDA received 11 comments on the revised draft guidance, including one comment from allergy organizations. In their submission, the allergy organizations stated that they are very pleased that FDA has clarified, in the revised draft guidance that its reference to USP Chapter 797 refers to the current version of that chapter and not any future chapter. The allergy organizations’ other comments, such as those relating to allergen extracts used for intradermal testing and the distribution of prescription sets, will be taken into consideration as FDA works on finalizing its guidance.

14. Duchenne Muscular Dystrophy

The Committee is encouraged that the FDA has the tools, authorities, and latitude necessary to review and approve safe and effective treatments for rare diseases, such as Duchenne Muscular Dystrophy, as efficiently as possible. In particular, the Committee is aware that the use of intermediate clinical endpoints (ICE) may be an appropriate approach as it has been in similar deadly diseases with dire unmet needs, such as HIV and cancer.

FDA Response:

FDA is committed to engaging with patient groups to receive valuable input during the evaluation of the medical needs of patients with rare diseases whenever appropriate. We appreciate the proposed guidance that members of the Duchenne muscular dystrophy (DMD) community submitted to FDA in June 2014. FDA announced the DMD community's guidance through a Federal Register notice (September 4, 2014) to seek additional input and public comment. FDA carefully considered the community's guidance and public comments received in response to it in writing the agency's own draft guidance.

The draft guidance for industry, "Duchenne Muscular Dystrophy and Related Dystrophinopathies: Developing Drugs for Treatment," was released in June 2015, and a 60-day comment period was provided. We are currently reviewing the comments received and plan to issue a final guidance following review of those comments. The purpose of the guidance to industry is to assist sponsors in the clinical development of drugs for treating X-linked Duchenne muscular dystrophy and related dystrophinopathies, discuss various pathways to approval including the use of intermediate clinical endpoints, and to serve as a focus for continued discussions on this topic.

15. Emerging Public Health Threat Funding

In order for the FDA to mount as rapid a response as possible to the spread of the Zika virus, the Committee reinforces its position that the agency obligate unobligated Ebola funds for the higher threat of Zika. The legislative text of the fiscal year 2015 emergency supplemental provided the FDA with such flexibility to deal with future public health emergencies such as those threats associated with the Zika viruses. Due to ongoing threats, the bill includes an appropriation of \$10,000,000 to support needs related to work on Ebola and Zika, such as support for FDA staff conducting ongoing response activities; support for regulatory science research to develop the tools, standards, and approaches to characterize investigational medical product safety, efficacy, quality, and performance; and support to expedite the development and availability of medical products for Ebola and Zika.

FDA Response:

The FDA reallocated \$4,975,000 of its Ebola emergency funding resources to support its response to the Zika virus outbreak. The FDA appreciates the inclusion of \$10,000,000 to support needs related to work on Ebola and Zika and would use this funding for further response activities including supporting the development and availability of medical countermeasures.

16. FDA and Centers for Medicare and Medicaid Services (CMS) Parallel Review Pilot

The Committee directs the FDA to provide a report within 60 days of enactment of this Act on whether it plans to once again extend the pilot and steps the agency will take to encourage more manufacturers to utilize the pilot, including considerations for manufacturers choosing the 510(k) approval pathway and for novel products deemed covered by CMS but that warrant evaluation to ensure the appropriate level of coverage. The Committee also directs the FDA to report on efforts to work with CMS to balance each agency's evidentiary needs with the burden on manufacturers, including the consideration and use of alternative trial designs.

FDA Response:

FDA and CMS have made the pilot Parallel Review Program into a permanent program, as stated in the published guidance 81 FR 73113-15 (Oct. 24, 2016). CMS, rather than FDA, determines the appropriate level of coverage. FDA and CMS continue to work together to balance sponsor evidence requirements to find the least burdensome approach to evidence collection.

17. FDA Partnerships under FSMA

The purpose of FSMA is to reform the nation's food safety laws to ensure a safe public food supply. As the FDA continues implementation of FSMA, the Committee encourages the FDA to work in partnership with existing government food safety programs, including the use of MOUs, to verify compliance with FSMA rules once they are finalized as a way to eliminate duplication of activities under the law. In addition, the Committee continues to provide \$5,000,000 for the Food Safety Outreach Program under NIFA and expects that NIFA will serve as the sole agency providing food safety training, education, outreach, and technical assistance at the farm level.

FDA Response:

FDA agrees that a strong partnership with other Federal, State, local, tribal, and territorial food programs is critical to achieving high rates of compliance with the FDA Food Safety Modernization Act (FSMA) and other existing food safety laws and regulations. FDA is committed to continuing our strong partnership with existing government food safety programs to implement FSMA and achieve an Integrated Food Safety System. FDA will continue to use Memoranda of Understanding with regulatory partners such as state, local, territorial, and tribal officials, in addition to contracts, grants, and cooperative agreements and other vehicles for partnership. FDA and NIFA have provided funding through grants for the National Food Safety Training, Education, Extension, Outreach, and Technical Assistance Grant Program. Grants to establish Regional Centers for Food Safety Training, Outreach and Technical Assistance were awarded to University of Florida Gainesville, Oregon State University, Iowa State University, and University of Vermont and State Agricultural College to provide food safety training, education, outreach, and technical assistance at the farm level. A grant to establish the National Coordination Center, coordinating with the Regional Centers, was awarded to the International Food Protection Training Institute in Battle Creek, Michigan. Both FDA and NIFA will continue to work with Regional Centers and the National Coordination Center to advance knowledge among food producers to meet FSMA requirements.

18. Federal Employee Conduct

The federal government grants federal employees with tremendous responsibility and trust to carry out their duties. They must do so free from conflicts of interest and without seeking private gain. Employees are public servants charged with implementing federal programs in a legal and ethical manner. Federal employees are reminded that they shall not advance a personal agenda or give preferential treatment to any outside organization or individual within government programs in which they administer. Information that is received by the employee, including information from the employees, offices, or Committees of the Congress of the United States, should be handled in a professional and confidential manner according to the federal government's code of conduct, standards, regulations, and statutes. The Committee is aware of

recent conduct in violation of these principles, and the Committee believes that it is incumbent upon agency officials to take immediate disciplinary action when they confirm such behavior.

FDA Response:

The agency continues to strengthen its ethics and integrity program to help employees avoid conflicts of interest. The agency is committed to preventive activities, such as continuing awareness campaigns of ethics standards for employees and in depth training to supervisors and managers to avoid conflicts. Additionally, the agency has established recommended actions when behavior in violation of these principles has been confirmed.

19. Food Contact Notification User Fees

The funds made available by this Act include sufficient monies to fund the FDA's Food Contact Notification Program and shall be deemed to satisfy the requirements of 21 U.S.C. 348(h)(5)(A). The Committee recommendation does not include proposed user fees.

FDA Response:

FDA acknowledges the Committee's recommendation on the proposed user fees.

20. Genomic Editing

The Committee understands the potential benefits to society in the genetic modification of living organisms. However, researchers do not yet fully understand all the possible side effects of editing the genes of a human embryo. Editing of the human germ line may involve serious and unquantifiable safety and ethical issues. Federal and non-federal organizations such as the National Academy of Sciences and National Academy of Medicine continue to understand the potential risks of genome editing and a broader public discussion of the societal and ethical implications of this technique is still ongoing. In accordance with the current policy at the National Institutes of Health, the Committee includes bill language that places a prohibition on the FDA's use of funds involving the genetic modification of a human embryo. The Committee continues to support a wide range of innovations in biomedical research, but will do so in a fashion that reflects well-established scientific and ethical principles.

FDA Response:

FDA currently does not accept investigational new drug applications in which a human embryo is intentionally created or modified to include a heritable genetic modification. FDA continues to work with organizations, such as the National Academies of Sciences, Engineering, and Medicine, to understand the scientific, medical, societal, and ethical implications of human germ line gene editing.

21. Harm Reduction

It is the Committee recommendation that the FDA consider the benefits of harm reduction as part of evaluations under the Deeming regulations for tobacco products.

FDA Response:

FDA recognizes that there is a continuum of risk for users of tobacco products. The agency will rely on sound science to evaluate the public health impact of new FDA-regulated tobacco products. The Agency has taken multiple actions concerning harm reduction. These actions include issuing draft guidance on modified risk tobacco products and soliciting comments on the continuum of risk and how it should impact regulatory policy. The concept of risk also plays a role in the agency's evaluation of new products. For example, premarket tobacco applications are to include information about investigations on the health risks of the new tobacco product and whether that tobacco product presents *less risk than other tobacco products*. The agency's evaluation of these applications includes an assessment of the risks and benefits to the population as a whole including users and nonusers of the tobacco product, and takes into account the increased or decreased likelihood of initiation and cessation. FDA reviewed premarket tobacco applications and issued marketing orders for eight snus smokeless tobacco products marketed by Swedish Match North America Inc. under the General brand name. FDA determined that these products would result in a low likelihood of new initiation, delayed cessation, or relapse, and that these products would likely provide less toxic options if current adult smokeless tobacco users used them exclusively.

FDA also has a regulatory pathway for tobacco products that are sold or distributed to reduce harm or the risk of tobacco-related disease. This includes products whose label, labeling, or advertising represents – explicitly or implicitly – that the product is less harmful or presents a lower risk of tobacco-related disease than one or more other commercially marketed tobacco products, or that the product or its smoke contains a reduced level of, presents a reduced exposure to, or does not contain, or is free of a substance. Under Section 911 of the Federal Food, Drug, and Cosmetic Act, FDA has authority to issue an order authorizing a product to be marketed as a modified risk tobacco product if the product will, or is expected to, benefit the health of the population as a whole, taking into account a number of factors including the relative health risks to individuals of the product, the likelihood that existing users of tobacco products who would otherwise stop using such products will switch to the product, and the likelihood that persons who do not use tobacco products will start using the product.

Applicants seeking a risk modification order under Section 911(g)(1) must demonstrate that the product, as actually used by consumers, will significantly reduce harm and the risk of tobacco-related disease to individual tobacco users and will benefit the health of the population as a whole.

Applicants seeking an exposure modification order under Section 911(g)(2) must demonstrate, among other things, that the product as actually used exposes consumers to the specified reduced level of the harmful substances and generally will not expose them to higher levels of other harmful substances, that consumers will not be misled by the product's labeling/marketing into believing the product has been shown to be less harmful and that the issuance of the order is expected to benefit the health of the population as a whole.

If the modified risk tobacco product is a new tobacco product within the meaning of section 910(a)(1), any applicable premarket review requirements under section 910 of the FD&C Act must also be satisfied.

22. Indoor Tanning Devices

Last December, the FDA proposed two rules intended to prevent the use of sunlamp products, including tanning beds, by certain age groups, reduce the risks for adults using these devices, and require manufacturers to take additional safety precautions. While the Committee remains deeply concerned with the deadly threat of melanoma, it questions some elements of the proposed rules. In particular, the Committee requests that the FDA hold a meeting with industry officials as it begins to consider the final regulations to discuss such issues as the number of allowable visits by adults and other similar measures that could create an undue economic burden on the industry.

FDA Response:

Sunlamp products, which include tanning beds and tanning booths, emit UV radiation that can cause skin cancer. According to the American Academy of Dermatology, people who have been exposed to UV radiation from indoor tanning before age 35 experience a 59 percent increase in the risk of developing melanoma, the deadliest type of skin cancer. This risk increases each time a person uses a sunlamp product, and is higher for younger users. FDA's proposed rules are intended to protect Americans, especially those under 18 years, from skin cancer and other illness or injury. The proposed rules are also intended to help ensure that adults make decisions regarding sunlamp product use based on accurate information. The Agency met in person with manufacturers of indoor tanning equipment while it drafted the rules. FDA looks forward to working with the new Administration on this issue and remains open to additional meetings with industry officials.

23. Late Reports

The Committee reminds the Commissioner that the timelines specified by the Committees on Appropriations of the House and Senate for fiscal year 2016 reports are deadlines that must be met. While the Committee notes that the FDA has made progress in providing more timely information and updates, the FDA still has several outstanding reports that are delayed due to long reviews and clearances. The Committee directs the Commissioner to submit these overdue reports.

FDA Response:

FDA will provide the requested reports.

24. Local Port Cooperation

The Committee directs the FDA to work with local governments at high volume ports of entry to explore activities which reduce the risk of food borne illnesses and enhance the capacity of local officials in dealing with food borne threats.

FDA Response:

FDA's Office of Regulatory Affairs (ORA) works extensively with local ports by directly engaging the local port authorities and U.S. Customs and Border Protection (CBP) and other partner government agencies (PGAs) to examine and control FDA-regulated food products at and around ports of entry. ORA also works with state and local governments on foodborne illness outbreaks, investigations, and appropriate follow-up activities. Additionally, FDA looks at not only volume of entries entering through a port, but also at the risk associated with those entries. The development and implementation of the Foreign Supplier Verification Program (FSVP) regulation and the Voluntary Qualified Importer Program (VQIP), both system-focused, risk-based programs adopted in accordance with the FDA Food Safety Modernization Act (FSMA), will help improve the safety of imported food products and maximize resources at all ports of entry.

25. Mammography Exam Reports

More than four years ago, in November 2011, the National Mammography Quality Assurance Advisory Committee approved a change to the mammogram patient report and physician report to include information regarding an individual's breast density. This process has not been completed. The Committee urges the FDA to implement this change in an expedited manner and must report to Congress on the status of this change no more than 60 days from the enactment of this Act.

FDA Response:

FDA is working with the Administration on this issue and will provide any requested report.

26. Medical Countermeasures

The Committee directs that not less than \$24,552,000 shall be available for the FDA's Medical Countermeasures Initiative. This total is in addition to the unobligated funds remaining to support the FDA's emergency response to Ebola and related disease outbreaks.

FDA Response:

FDA intends to spend the amount directed by the Committee on the activities outlined.

27. Medical Gas Rulemaking

The Committee is significantly concerned that the FDA has not initiated rulemaking to address numerous longstanding regulatory issues for medical gases despite the statutory requirement in the Food and Drug Administration Safety and Innovation Act (FDASIA) to issue a final rulemaking addressing all necessary changes for medical gases by July 9, 2016. In fact, the FDA rulemaking on medical gases is not even listed in the most recent Unified Agenda as a priority.

Designated medical gases are a unique class of drugs that differ significantly from traditional pharmaceuticals and therefore must be addressed in the federal drug regulations to prevent safety and enforcement issues caused by current regulations. The Committee disagrees with the FDA report to Congress sent on June 30, 2015, which stated that, despite decades of issues created by existing regulations, “the current regulatory framework is adequate and sufficiently flexible to appropriately regulate medical gases.” The bill includes language requiring the FDA to issue final regulations revising the federal drug regulations with respect to medical gases not later than July 9, 2016. If the Commissioner fails to issue final regulations with respect to medical gases by the statutory deadline, the Commissioner shall incorporate by reference voluntary consensus safety and labeling standards developed by an ANSI-accredited standard development organization until such time as the Commissioner issues final regulations consistent with Section 1112 of Public Law 112–144.

FDA Response:

FDA issued the final rule “Medical Gas Containers and Closures: Current Good Manufacturing Practice Requirements,” on November 18, 2016 (81 FR 81685). This final rule (which revised warning statements for medical gases and required measures intended to reduce the likelihood of medical gas mix-ups) satisfies the FDASIA medical gas rulemaking requirement, though FDA may undertake additional rulemaking on medical gases as needed.

FDA understands that industry stakeholders believe that FDA should promulgate a separate regulatory scheme specific to medical gases, despite the Agency’s determination (explained in its 2015 report to Congress on this topic) that extensive rulemaking in this area is unnecessary. However, FDA remains convinced that we can work within the existing regulatory framework to set clear and appropriate regulatory expectations for the production and distribution of medical gases without extensive additional rulemaking. FDA recently made revisions to the medical gas inspection program (completed in 2015), and is very far along in the process of producing revised guidance on current good manufacturing practices applicable to medical gases.

FDA will, of course, undertake targeted rulemaking on medical gases to address any significant public health issues that arise, or to satisfy statutory rulemaking requirements – as demonstrated by the final rule published in November 2016. However, FDA continues to believe that the separate regulatory scheme for medical gases sought by industry stakeholders is unnecessary.

FDA also has significant concerns with any proposal mandating that FDA incorporate medical gas industry standards by reference. First, incorporation by reference requires notice-and-comment rulemaking, with all of the resource burdens rulemaking entails. Furthermore, the proposal to incorporate by reference “voluntary consensus safety and labeling standards” would first require such standards to be developed, as it does not appear that any currently exist. Rather, the safety and labeling standards industry has sought to have FDA incorporate by reference were created entirely by the industry, with no FDA involvement. In fact, these “standards” are largely identical to the dozens of new regulations industry proposed during the 2013 FDASIA regulation review, and which FDA determined were generally not needed. FDA is not opposed to referencing specific targeted standards co-developed by FDA and the medical gas industry (provided FDA agrees such standards meet regulatory and public health needs) and engaging in rulemaking as necessary and appropriate. However, FDA sees significant legal, policy, logistical, and resource concerns with adopting unvetted industry standards by reference.

Finally, FDA is concerned with the precedent that would be set by creating a separate regulatory scheme for a given product class. In general, FDA believes it is much more efficient to rely upon the general regulatory scheme applicable to all drug products and to provide class-specific recommendations through guidance and other non-rule-making means.

Accordingly, FDA's position continues to be that the extensive rulemaking sought by industry is not necessary.

28. Laboratories Near High Volume Ports (ORA)

The Committee directs the FDA to submit a report within 90 days of enactment of this Act on the potential for implementing pilot programs which will allow for public-private partnerships at high volume ports of entry in an effort to increase the number of FDA-certified public or private labs located near major ports of entry to provide services on weekends and holidays, reduce the risk of food borne illnesses, and enhance the capacity of local officials in dealing with foodborne threats.

FDA Response:

Currently, FDA does not certify laboratories. However, consistent with section 202 of FSMA, FDA is developing a program for the accreditation of laboratories for analyses of foods. FDA is currently engaged in the rulemaking process for this laboratory accreditation program. Establishing a separate laboratory certification program could be duplicative of the FSMA laboratory accreditation program and divert resources from FDA's implementation of this FSMA provision.

Additionally, it is not clear if the intent is to use the results from these laboratories to support FDA regulatory activities, e.g., to institute a seizure action against a product already in U.S. commerce, or to assist in the surveillance sampling and testing performed by FDA laboratories on foods offered for import to determine admissibility. If the intent is for private laboratories to perform analyses used to support regulatory activities by FDA, there would be many issues to consider.

FDA has previously evaluated the proximity to port issue, including the establishment of satellite laboratories co-located in ports of entry, with limited capabilities for analysis. However, given the increasing complexities of required analyses for imported products and the necessity for rapid screening methodologies that also require greater sensitivities and lower limits of detection, most of this work must be done in a larger, fixed-site, fully functioning laboratory. FDA ORA laboratories currently do maintain weekend schedules which provide weekend capacity to address urgent events.

29. Laboratory Developed Tests

The FDA's draft guidance issued on October 3, 2014, titled "Framework for Regulatory Oversight of Laboratory Developed Tests" (LDTs), puts forth a proposed regulatory framework that is a significant shift in the way LDTs are regulated. Such a shift deserves input from the public, and Congress has been working with stakeholders, constituencies, and the FDA to find common ground on regulating LDTs. The FDA's guidance circumvents the normal rulemaking process and changes expectations for patients, doctors, and laboratories for the first time since

the Clinical Laboratory Improvement Amendments Act was passed in 1988. The Committee directs the FDA to suspend further efforts to finalize the LDT guidance and continue working with Congress to pass legislation that addresses a new pathway for regulation of LDTs in a transparent manner.

FDA Response:

FDA appreciates that this topic is of great interest to the Committee members and stakeholders. We would welcome the opportunity to review any legislative proposals from Members of Congress.

30. Medical Device Facility Inspections

The Committee is concerned about the lack of transparency and consistency with the medical device facility inspection process. This often leads to inefficiencies and inconsistencies in the inspection process. The Committee urges the agency to work with stakeholders and Congress to improve the facility inspection process. Potential process improvements may include, but are not necessarily limited to, more timely and frequent communications related to inspection observations and remediation plans, as well as changes to the way medical device Export Certificates (e.g., Certificate to Foreign Government, etc.) are affected by FDA Observational Findings following a facility inspection. In addition, the agency shall produce a report to the Committee by September 30, 2016, which provides information on the rates of inspection for facilities across districts and internationally and any FDA efforts to standardize rates of inspections across districts and internationally. The Committee understands that five days is typically sufficient for the FDA to complete an overseas inspection and determine the suitability of the location to provide product into the U.S. market while inspections inside the U.S. can take several weeks or months to complete the same assessment. These discrepancies lead to variations in inspection standards and potentially competitive advantages for those who choose to manufacture outside the U.S.

FDA Response:

A majority of both domestic and foreign device inspections involve four or fewer days on-site. There are many device inspections that conclude on the same day as arrival. Domestic inspections can take longer than foreign inspections. Foreign inspections are planned for consecutive days (excluding weekends) and more hours are spent at the firm per day than a domestic inspection, while on a domestic inspection an investigator may be completing an inspection over non-consecutive days. FDA has indicated its willingness to hold a public meeting to gather input from affected stakeholders about improvements to the device inspections process. FDA is working with HHS to review legislative proposals intended to help streamline the device inspections process.

FDA is currently addressing domestic inspection times through improved internal procedures and through Program Alignment, which will take effect on May 15, 2017. Program Alignment is FDA's reorganization of its inspection program to a commodity-based and vertically integrated structure such that, for example, only device specialists will inspect device establishments and drug specialists will inspect drug establishments.

31. Menu Labeling

The Committee is concerned about the recent FDA final determination that increased the size and scope of those affected under restaurant menu labeling regulations. Specifically, the final rule attempts to regulate local grocery chains that typically do not qualify as restaurants. The Committee includes bill language which directs the FDA to implement the final rule no earlier than December 1, 2016, at least one-year following agency publication of related guidance to newly regulated stakeholders.

FDA Response:

FDA issued a final guidance document on May 5, 2016, to help covered establishments comply with the menu labeling final rule, which requires calorie information to be listed on menus and menu boards in chain restaurants and similar retail food establishments with 20 or more locations doing business under the same name and offering for sale substantially the same menu items. The final guidance responds to many of the most frequently asked questions the agency has received through extensive input from stakeholders throughout the process of establishing requirements for menu labeling in certain restaurants and other retail food establishments and to the substantive and useful feedback in the stakeholder comments on the draft guidance published in September 2015.

In December 2016, FDA extended the compliance date for these covered establishments to May 5, 2017, one year after FDA issued the menu labeling final guidance, to ensure that companies have adequate time to fully implement the requirements of the rule.

On May 1, 2017, FDA announced it was extending the compliance date for menu labeling requirements from May 5, 2017 to May 7, 2018.

32. Nanotechnology

The Committee recognizes the increased capabilities that the FDA has developed to study environment, health, and safety of nanomaterials within the FDA's Jefferson Laboratory Campus, including the National Center for Toxicological Research, and its consolidated headquarters at White Oak, Maryland. The Committee recommends continued collaborative research with universities and industry on the toxicology of nanotechnology products and processes, in accordance with the National Nanotechnology Initiative Environment, Health, and Safety Research Strategy as updated in October 2011.

FDA Response:

FDA continues to enhance capabilities to understand the health impact and safety of nanomaterials through staff training, continued research into the safety and disposition of nanomaterials in various products, increased collaboration with government agencies — both national and international — and participation in standards-development activities. FDA continues its efforts to enhance its nanomaterials research infrastructure. Since 2011, the Collaborative Opportunities for Research Excellence in Science (CORES) research program funded a total of 36 projects and is part of FDA's Nanotechnology Regulatory Science Research Plan. Together with the advanced Nanocore infrastructure at the Jefferson Laboratories campus and facilities at the White Oak campus, FDA is able to conduct research to accurately characterize, detect, and quantify nanomaterial in FDA-regulated products to help assess safety

and inform risk assessment. FDA's Nanotechnology Task Force is committed to advancing nanotechnology research and collaboration.

FDA continues to engage with industry and other agencies through the National Nanotechnology Initiative (NNI), including participation in the US-EU Communities of Research, Indo-US Science and Technology Forum, Nanotechnology for Healthcare Conference, and collaborations with the Consumer Protection Safety Commission, National Institute of Environmental Health Sciences/National Toxicology Program, and the National Cancer Institute.

The 2016 Global Summit on Regulatory Science focused on "Nanotechnology Standards and Applications" and was hosted by FDA/NCTR and Arkansas Research Alliance. There were other U.S. government agencies in attendance at the Summit — held on the NIH campus — as well as participants from 19 countries. This annual Summit is held in cooperation with the European Union and global regulatory and standards agencies to discuss the standards methodologies and standards that are helpful for regulatory reviews. The outcome from the 2016 Summit was a list of standards in nanotechnology that are relevant to drugs, devices, and consumer products. FDA will also continue to engage industry through the standards-development organizations to help develop relevant and consensus based standards that can help regulatory reviews.

33. Nutrient Content Claims

The Committee expects the FDA to amend its "healthy" nutrient content claim regulation to be based upon significant scientific agreement. In addition, to ensure that food producers can make truthful and non-misleading statements about the healthfulness of products, the Committee directs the FDA to make such regulatory changes during the rulemaking process and issue guidance to industry no more than six months after the enactment of this Act providing for the use of the word "healthy" in food labeling statements.

FDA Response:

FDA is currently engaged in updating nutrition labeling regulations to reflect the latest consensus nutrition science, including the 2015-2020 *Dietary Guidelines for Americans*. As the first step, in May 2016, FDA published a final rule updating the Nutrition Facts label regulations to reflect the latest science. Among other updates to nutrition labeling regulations, FDA is considering whether and how to redefine the nutrient content claim "healthy." FDA is aware that the current definition for "healthy" needs to be updated in order to be consistent with the latest science, and will work collaboratively with all stakeholders in this process, including food producers.

As background, on September 28, 2016, FDA started a public process to solicit stakeholder input on whether and how to redefine the "healthy" nutrient content claim. We published a request for information and comments in the *Federal Register* and issued a guidance document stating that while we consider revisions to the claim, we do not intend to enforce certain current eligibility requirements relating to use of the claim if specific criteria are met. For example, the current regulation requires that foods bearing a "healthy" claim limit the amount of total fat. However, current science shows that the type of fat is more important than the total amount of fat. Additionally, the current regulation for a "healthy" claim requires specific criteria for nutrients to limit, in addition to total fat, such saturated fat, cholesterol, and sodium, as well as requirements for nutrients to encourage, including vitamin A, vitamin C, calcium, iron, protein, and fiber.

These criteria are linked to elements in the Nutrition Facts label regulations. However, the 2016 revision to the Nutrition Facts label requires the declaration and Daily Values for potassium and vitamin D; Vitamins A and C are no longer mandated on the label. Consequently, the guidance on “healthy” advises food manufacturers of our intent to exercise enforcement discretion relative to foods that use the implied nutrient content claim “healthy” on their labels which: (1) are not low in total fat, but have a fat profile makeup of predominantly mono- and polyunsaturated fats; or (2) contain at least 10 percent of the Daily Value per reference amount customarily consumed of potassium or vitamin D.

On December 30, 2016, we extended the comment period to allow more time for public comment on the definition of the term “healthy.” On March 9, 2017, FDA held a public meeting to give interested parties an opportunity to discuss and provide feedback on the use of the term “healthy” on food labels. The information shared during the meeting and throughout the comment period, which closed on April 26, 2017, will help us determine how to proceed with this matter.

34. Nutrition Facts Label

The Committee is concerned that proposed rules that have been issued to revise the Nutrition and Supplemental Facts labels may create confusion and misinformation among consumers. The FDA is encouraged to determine how the proposed new label disclosure statements regarding added sugars would be understood and interpreted by consumers before proceeding with a final rule. Additionally, the FDA should evaluate the consumer perception and impact on healthful nutrient dense foods that use added sugar to make the food more palatable.

FDA Response:

In May 2016, FDA published the final rule for the Nutrition and Supplement Facts labels, in which, after consideration of comments, FDA finalized a declaration requirement for added sugars. FDA required the declaration for added sugars, in part, because excess consumption of added sugars makes it difficult to meet nutrient needs while staying within calorie limits, and can lead to an increase in overall caloric intake. Further, healthy dietary patterns with lower amounts of sugar-sweetened foods and beverages, when compared to less healthy dietary patterns, are associated with a reduced risk of cardiovascular disease.

In collaboration with Federal and other partners, FDA plans to engage in educational activities for consumers and health professionals about the use of information on the Nutrition Facts label. Part of that education will include information about added sugars. A key message related to added sugars will be that consumers should consider all of the information on the Nutrition Facts label when constructing a healthful dietary pattern. Further, a key message will be to moderate—rather than eliminate—intake of added sugars. If consumers choose to eat foods with sugars added to them, for example, for palatability, they may do so in moderation, and cut back on added sugars elsewhere in the diet.

35. Office of Cosmetics and Colors

The Committee recommendation includes not less than \$11,700,000 for cosmetics activities, including not less than \$7,200,000 for the Office of Cosmetics and Colors (OCAC) and other supporting offices within the Center for Food Safety and Applied Nutrition (CFSAN). Funding provided for CFSAN is for direct support of operation, staffing, compliance, research and international activities. The Committee notes that every year since fiscal year 2012 it has requested that OCAC respond to a citizen petition setting safety levels for trace amounts of lead in cosmetics. The Committee is disappointed that OCAC has not responded to these requests and urges OCAC to make this a priority. Therefore, the Committee directs OCAC to respond to the petition by September 15, 2016.

The Committee appreciates OCAC's willingness to engage with China in 2016 for a cosmetics regulatory dialogue. In light of China's importance to U.S.-based manufacturers and consumers, the Committee directs the FDA to seek ways to continually enhance engagement with Chinese regulators on cosmetic technical and regulatory issues. The Committee directs the FDA to promote international regulatory harmonization and trade in cosmetic products by supporting international trade negotiations on cosmetics in the Transatlantic Trade and Investment Partnership, the International Cooperation on Cosmetics Regulation (ICCR), and other bilateral and multilateral trade agreements.

FDA Response:

CFSAN will use funding for direct support of the operation, staffing, compliance, research, and international activities.

After completing testing of a selection of cosmetics products and performing an exposure assessment, FDA granted the Personal Care Products Council's Citizen Petition on December 22, 2016. On that same day, FDA issued draft guidance for industry recommending a limit of no more than 10 parts per million (ppm) for lead as an impurity in cosmetic lip products (such as lipsticks, lip glosses, and lip liners) and externally applied cosmetics (such as eye shadows, blushes, compact powders, shampoos, and body lotions), based on our assessment that the recommended maximum lead level would not pose a health risk. FDA considers the recommended maximum lead level to be achievable with the use of good manufacturing practices and consistent with the 10 ppm maximum lead level for similar products recommended by other countries.

In May 2016, FDA, with representation from OCAC, participated in the US-China Joint Commission on Commerce and Trade dialogues with China Food and Drug Administration (CFDA), General Administration of Quality Supervision, Inspection and Quarantine (AQSIQ), and other agencies in Beijing, China. This meeting was to establish communications among regulators on topics of mutual interest as well as to engage in discussions about trade-related issues. FDA continues to maintain an interactive dialogue with China on technical and regulatory issues, including animal testing and compliance/enforcement issues.

FDA has supported international trade negotiations and regulatory harmonization for several years—e.g., through participation in the international group of cosmetics regulatory authorities called International Cooperation on Cosmetics Regulation (ICCR) and engagement in discussions in support of various trade negotiations and bilateral discussions with other countries, such as China, Brazil, and Canada. FDA will continue to identify opportunities to

further these goals—for example, by providing technical assistance in support of the U.S. Government’s international trade negotiations and by engagement with the ICCR to the extent that resources and priorities allow.

36. Olive Oil

The Committee is concerned with reports that consistently describe the prevalence of adulterated and fraudulently labeled olive oil imported into the United States and sold to American consumers. In addition, some products labeled as olive oil may contain seed oil, which poses a serious health risk to consumers who are allergic to seed oil. The Committee directs the FDA to take a sampling of imported olive oil to determine if it is adulterated or misbranded, pursuant to Section 342 or Section 343 of the FDCA, respectively, and report to Congress within 270 days on its findings and what actions the FDA will take to ensure consumer safety and proper labeling of imported olive oil.

FDA Response:

In 2014, FDA performed a survey of olive oil products available to consumers within the United States, and included a cross-section of domestic and imported products in the survey. FDA used USDA grading standards in the assessment and used an analytical methodology capable of detecting 10 percent seed oil adulteration. Out of 88 products surveyed, only three showed evidence of adulteration. This work was published in a peer-reviewed publication^{1,2}. FDA continues to develop better methods that may be able to detect adulteration beyond gross addition of seed oils^{3,4}. FDA plans to continue to monitor the marketplace for adulterated olive oil products to ensure consumer safety and proper labeling of imported olive oil.

1. Authenticity Assessment of Extra Virgin Olive Oil: Evaluation of Desmethylsterols and Triterpene Dialcohols; Srigley, CT; Oles, CJ; Kia, ARF; Mossoba, MM; JOURNAL OF THE AMERICAN OIL CHEMISTS SOCIETY; 93(2); 2016; pp: 171-181. (DOI: 10.1007/s11746-015-2759-4)
2. Authenticity Assessment of Extra Virgin Olive Oil, part 2. Evaluation of fatty acids and triacylglycerols; manuscript in preparation, 2017.
3. Nontargeted, Rapid Screening of Extra Virgin Olive Oil Products for Authenticity Using Near-Infrared Spectroscopy in Combination with Conformity Index and Multivariate Statistical Analyses; Karunathilaka, SR; Kia, ARF; Srigley, C (Srigley, Cynthia); Chung, JK; Mossoba, MM; JOURNAL OF FOOD SCIENCE; 81(10); 2016; pp C2390-C2397. DOI: 10.1111/1750-3841.13432
4. Developing FT-NIR and PLS1 Methodology for Predicting Adulteration in Representative Varieties/Blends of Extra Virgin Olive Oils; Azizian, H; Mossoba, MM ; Fardin-Kia, AR ; Karunathilaka, SR; Kramer, JKG; LIPIDS; 51(11); 2016, pp 1309-1321 (DOI: 10.1007/s11745-016-4195-0).

37. Opioid Abuse

The abuse, misuse, and diversion of opioid painkillers has precipitated an epidemic in the United States. The CDC indicates that one American loses his or her battle with addiction every twenty minutes. For years, the Committee has encouraged the FDA to utilize the full breadth of its regulatory authority to address this challenge. The Committee is pleased that, with the Opioids Action Plan, the FDA has acknowledged that the agency shoulders some responsibility for turning the tide of abuse. The FDA's recent regulatory changes related to scheduling and labeling of opioids are positive developments, as are efforts to encourage the development of abuse-deterrent formulations (ADF) and new evidence-based medication-assisted therapies (MAT).

The use of opioids as first-line therapies for any form of pain has led to over-prescribing, and the CDC has made clear that clinicians should consider opioid therapy only if expected benefits for both pain and function are anticipated to outweigh the risks to the patient. With respect to prescribing patterns, the Committee supports efforts to incentivize ADF use by clinicians and to increase the number of prescribers who receive training on pain management and safe prescribing of opioid drugs in order to decrease inappropriate opioid prescribing. The Committee notes that 38,370 Extended Release/Long-Acting (ER/LA) opioid analgesic prescribers have been trained through the FDA's Risk Evaluation and Mitigation Strategy (REMS), but is disappointed that this constitutes less than half of the 80,000 prescriber training goal that was established in 2012. Even if the FDA was on track to meet its lofty goal of having 60 percent of ER/LA prescribed take a REMS class by 2017, there will still be some 128,000 prescribers without additional, opioid-specific training. The Committee understands that FDA intends to share these lackluster results with an advisory committee to assess its impact on preventing the misuse and abuse of opioids, and to determine what changes, if any, need to be made to the program.

The Committee notes that treatment is not a "one size, fits all" enterprise and that every patient's treatment regimen should be tailored by his or her doctor to his or her unique needs. The federal government, therefore, ought to be promoting the full suite of available treatment options—including abstinence-based models and non-opioid medications—rather than picking winners and losers. The Committee supports efforts at the FDA and elsewhere to develop MATs that improve efficacy of daily administration, are resistant to diversion and misuse, and/or help patients on a path to abstinence. Finally, the Committee has been supportive of naloxone distribution and training licensed healthcare professionals and emergency responders on its use. When considering the appropriateness of providing naloxone over the counter, the Committee asks the FDA to ensure that the administration of naloxone serves as a point of intervention to spur an honest conversation between the patient and his doctor about addiction and treatment.

FDA Response:

FDA remains committed to increasing the number of prescribers who receive training on pain management and safe prescribing of opioid drugs in order to decrease inappropriate opioid prescribing. FDA continues to explore potential methods to increase prescriber training, bearing in mind that clinicians may be receiving opioid prescribing education from sources other than training provided under the ER/LA Opioid Analgesics REMS, and accordingly is holding a public workshop, on May 9th and 10th, 2017, to obtain input on issues and challenges associated

with Federal efforts to support training on pain management and the safe use of opioids for health care providers.

This workshop has three main goals. Participants will be asked to 1) discuss the role that health care provider training plays, within the broader context of ongoing activities, to improve pain management and the safe use of opioids; 2) comment on how best to provide health care providers, who prescribe or are directly involved in the management or support of patients with pain, appropriate training in pain management and the safe use of opioids; and 3) comment on the issues and challenges associated with possible changes to Federal efforts to educate health care providers on pain management and the safe use of opioids.

FDA remains committed to promoting a comprehensive effort to combat opioid abuse, including supporting the development of MATs and the use of naloxone when appropriate. In May 2016, FDA approved probuphine, a first-of-kind subdermal implant for the maintenance treatment of opioid dependence, providing a new treatment option for patients struggling with opioid addiction. FDA has also approved in recent years both an auto-injector and an intranasal form of naloxone, which facilitate use by laypersons. Looking ahead, FDA is identifying ways to assist manufacturers in submitting an application to the FDA for an over-the-counter (OTC) version of a naloxone product. This assistance has included development of a consumer-friendly Drug Facts label (which is required for OTC drug products), and the award of a contract for a study currently being conducted on consumer understanding of how to use naloxone in the OTC setting.

38. Over-the-Counter (OTC) Monograph Resources

The Committee understands that, over the past few years, funding allocated to OTC monograph issues has declined, in part due to stagnation in rulemaking and timely responses to Citizen Petitions related to OTC Monograph ingredients. The FDA is directed to provide an exhibit within the fiscal year 2018 budget justification with the total obligations and staffing levels associated with OTC Monograph issues for the past 11 years (fiscal years 2006–2016). In addition, the FDA is directed to develop detailed justifications and supporting documentation if the agency proposes to increase funding or staffing levels with regard to reforms of the OTC process in future budget submissions.

FDA Response:

FDA will provide a response to Congress for this Significant Item in a supplemental package.

39. Packaged Ice

The Committee recognizes that packaged ice is produced in the U.S., traded internationally, and consumed as both a packaged food and a food ingredient. The FDA has had a citizen petition regarding a proposed standard of identity for packaged ice for a significant and unacceptable length of time and is directed to provide quarterly status reports to the Committee on this effort until a response has been provided. Further, the Conference for Food Protection recently reviewed issues related to commercial ice machines in the retail environment and found that research is needed to identify the type of microbial growth and locations of concern within these

machines. Therefore, the FDA is directed to research the issue more carefully and establish a cleaning and sanitizing frequency standard for commercial ice machines.

FDA Response:

FDA is currently reviewing the citizen petition requesting establishment of a standard of identity and a standard of quality for packaged ice. However, due to other high-priority activities that merit the agency's immediate attention and limited resources, we have not been able to complete our review of the petition and issue a response.

Generally, a facility that manufactures, processes, packs, or holds packaged ice for human consumption is subject to subpart B (Current Good Manufacturing Practice) in FDA's Current Good Manufacturing Practice, Hazard Analysis, and Risk-Based Preventive Controls for Human Food regulations in 21 CFR part 117.¹⁰⁴ These regulations provide the appropriate standards for the preparation, packing and holding of packaged ice, including cleaning and sanitizing practices by FDA-regulated firms. In addition, under 21 CFR part 117, a facility is also subject to the requirements for hazard analysis and risk-based preventive controls in subpart C, unless an exemption applies. A covered facility must conduct a hazard analysis and implement preventive controls for hazards identified as requiring a preventive control.

FDA has issued a Food Facts sheet that addresses concerns raised by the International Packaged Ice Association (IPIA) regarding the lack of awareness of ice safety and of FDA's role in regulating packaged ice. This document is available at: www.fda.gov/Food/ResourcesForYou/Consumers/ucm197586.htm.

As explained in the Food Facts sheet, State and local regulators have the primary responsibility for regulating retail establishments and can use the FDA Food Code as a model to develop or update their own food safety regulations and to be consistent with national food regulatory policy. The Food Code contains many provisions relevant to production and handling of food and ice including the cleaning and sanitizing of food contact surfaces, potable water requirements, proper plumbing and backflow prevention for ice machines, proper labeling of packaged foods, and guidance on proper handling of ready-to-eat foods, including to not touch food with bare hands. In April 2016, the Council on Food Protection has recommended that FDA amend the FDA Food Code to address more specifically the cleaning frequency associated with equipment such as ice makers and other such equipment with enclosed components. In response, FDA is reviewing the Food Code language to determine if clarity surrounding the frequency of cleaning is best achieved through an interpretation of the existing Code language and placed in the online database of Food Code interpretations known as the Food Code Reference System (FCRS), or through making a change in the Code's language.

¹⁰⁴ The CGMP regulations in 21 CFR part 110 have been updated and included in 21 CFR part 117 as part of FDA's Food Safety Modernization Act rulemaking (see the final rule on "Current Good Manufacturing Practice, Hazard Analysis, and Risk-Based Preventive Controls for Human Food" (80 FR 55908, September 17, 2015)). Compliance dates for the provisions of 21 CFR part 117 are phased in based on size, with very small businesses having to comply on September 17, 2018, small businesses on September 18, 2017, and all other businesses on September 19, 2016. See 21 CFR 117.3 for definitions of business size.

40. Pediatric Devices

The Committee applauds the FDA's support of development of pediatric medical devices through the Pediatric Device Consortia and notes the significant investment of more than \$65,000,000 in non-FDA funding that consortia members have raised to advance pediatric device projects. The program funds consortia to assist innovators in developing medical and surgical devices designed for the unique needs of children that often go unmet by devices currently available on the market. The Committee provides an increase of \$2,500,000 in fiscal year 2017 for the consortium to better leverage federal investments and move more devices to the market. The Committee directs that the agency spend no less than \$6,000,000 in order to attract additional funds for these vital projects.

FDA Response:

The Pediatric Device Consortia (PDC) Grant Program continues to successfully support the development of pediatric medical devices and fulfill unmet needs in the pediatric population. Since the program's inception in 2009, the pediatric device consortia have advised innovators on more than 900 potential pediatric devices – and assisted on more than 300 projects just this past year alone. As a result of funding advice provided by the consortia, more than \$110 million of additional funds have been raised to advance pediatric device projects affiliated with the consortia. In the last 4 years, more than ten PDC-assisted pediatric medical devices have become available for use in pediatric care, including TIVA, a needle-free blood collection device, and SleepWeaver Advance Pediatric CPAP Mask. The FDA recognizes the value of the Pediatric Device Consortia in supporting the pediatric medical device ecosystem toward development and innovation for children. The FDA anticipates funding the PDC at the appropriated level for the upcoming year, consistent with prior years.

41. Pet Food Imports

As of September 2014, the FDA has received more than 5,800 complaints of illness related to consumption of chicken, duck, or sweet potato jerky treats, nearly all of which are imported from China. The reports involve more than 5,800 dogs, 25 cats, three humans and include more than 1,000 pet deaths. These incidents date back to 2007. The Committee requests that the FDA provide it with a timeline of all activities associated with the investigation into the pet illnesses associated these products, including any import alerts and import refusals, within 60 days of the enactment of this Act. In addition, the Committee requests that the agency provide it with semi-annual reports on the status of the investigation into these illnesses beginning in April 2016 and continuing until the issue has been resolved.

FDA Response:

FDA will provide the Committee with the requested timeline and report. We currently are assembling information for the FY 2017 annual report on the status of the investigation, as requested by the Committee. In the past two years, the FDA has noted a significant decline in the number of complaints associated with jerky pet treats, and accordingly is in the process of scaling back the investigation to focus on other pet food issues. We continue to monitor jerky pet treats and other pet food issues. The Agency continues to routinely post updates on the pet jerky treat investigation on its website to inform the public and other interested stakeholders about the Agency's actions and developments in the investigation. Please see the following link

for more information related to pet jerky treats:

www.fda.gov/AnimalVeterinary/SafetyHealth/ProductSafetyInformation/ucm360951.htm. For information on our laboratory activities, please see the following link:

www.fda.gov/AnimalVeterinary/ScienceResearch/ucm247334.htm#JerkyPetTreats.

42. Pharmacy Compounding

The Committee remains concerned with the draft MOU that the FDA proposed under Section 503A of the FDCA. Section 503A distinguishes between “distribution” and “dispensing” for the purposes of the MOU. In the DQSA, Congress only allowed the FDA to regulate “distribution”. The MOU appears to exceed the authority granted in the statute by redefining “distribution” in a manner that includes dispensing. Congress did not intend to include dispensing of compounded drugs over state lines within the scope of the MOU. The MOU should not address dispensing of compounded drugs to a patient over state lines if all other requirements of 503A are met.

FDA Response:

Section 503A of the FD&C Act describes the conditions that must be satisfied for a drug compounded by a licensed pharmacist in a State licensed pharmacy or Federal facility, or by a licensed physician, to qualify for exemptions from section 505 (concerning pre-market approval requirements), section 502(f)(1) (concerning labeling with adequate directions for use), and section 501(a)(2)(B) (concerning current good manufacturing practice requirements).

When Congress enacted the DQSA, it left intact as one of the conditions necessary to qualify for the exemptions listed in section 503A of the FD&C Act that:

(1) the drug product is compounded in a State that has entered into an MOU with FDA that addresses the distribution of inordinate amounts of compounded drug products interstate and provides for appropriate investigation by a State agency of complaints relating to compounded drug products distributed outside such State

(2) if the drug product is compounded in a State that has not entered into such an MOU, the licensed pharmacist, pharmacy, or physician does not distribute, or cause to be distributed, compounded drug products out of the State in which they are compounded in quantities that exceed 5 percent of the total prescription orders dispensed or distributed by such pharmacy or physician (see section 503A(b)(3)(B)(i) and (b)(3)(B)(ii) of the FD&C Act).

Even though the statute did not direct FDA to obtain public input on the draft standard MOU, other than the consultation with the National Association of Boards of Pharmacy (NABP), FDA has engaged in a public process to obtain comments on the draft standard MOU. FDA has solicited public input from the public generally through written comments to the docket, and has also discussed the proposed MOU with representatives from the 50 states.

FDA discussed the concepts it was considering for the MOU at an Intergovernmental Working Meeting with representatives of the 50 States and NABP in March, 2014. After the draft standard MOU was published for comment, FDA discussed the published draft at Intergovernmental Working Meetings with representatives of the 50 States in March, 2015, and again in November, 2015, after the comment period closed. FDA received over 3,000 comments to the docket on the draft MOU. FDA is considering all of the comments, including comments on the definition of “distribution,” as we work to finalize the MOU.

43. Premium Cigars

The Committee includes statutory language exempting premium and traditional large cigars, in keeping with FDA's intent under Option 2 of its proposed rule "Deeming Tobacco Products To Be Subject to the Federal Food, Drug, and Cosmetic Act, as Amended by the Family Smoking Prevention and Tobacco Control Act (TCA); Regulations on the Sale and Distribution of Tobacco Products and Required Warning Statements for Tobacco Products" (Docket No. FDA-2014-N-0189). The Committee notes that premium cigars are shown to be distinct from other tobacco products in their effects on youth initiation, the frequency of their use by youth and young adults, and other such behavioral and economic factors. Lastly, a large number of participants in this unique business are small and very small operations that might not be able to maintain jobs and a physical presence in the United States due to the financial impact of this pending regulatory burden. Given that there is very little mention of cigars throughout the TCA, it is clear Congress did not intend to focus on the unique subset of premium cigars.

FDA Response:

Left unchanged, Section 749 of H.R. 5054 (114th Congress) would prevent the Agency from using funds to finalize, implement, administer, or enforce the deeming rule if it applies to traditional large and premium cigars. If the language became law, FDA will no longer be able to implement the deeming rule, nor enforce any of the provisions in law or regulation for any of the newly deemed products regardless of the effective and compliance dates set forth by FDA in the rule and its preamble. This means that sales to youth will be legal again, as will free sampling of newly deemed tobacco products. None of the newly deemed products will be subject to FDA premarket review and FDA will be unable to set tobacco product standards for such products to protect public health.

We also note that the definition of "traditional large and premium cigar" is very broad and may include more products than the drafters intend, including products that could be attractive to youth.

44. Prescription Drug Labeling Inserts

The Committee is aware of FDA proposals that would subvert repeatedly expressed Congressional intent by permitting the distribution of prescription drugs without printed prescribing information on or within the packages from which such drugs are to be dispensed. The FDA intends to replace such printed labeling with an electronic labeling system for the majority of prescription drugs. On several occasions Congress has directly declined to provide the FDA the necessary statutory authority to implement this change. As recently as 2012, Congress commissioned a GAO report (GAO-13-592) discussing this issue. The GAO report concluded that such a change could adversely impact public health. Thus, the Committee is very concerned that the FDA is moving to promulgate a regulation that would generally eliminate printed prescribing information inserts for prescription drugs. Therefore, the Committee has included a provision prohibiting the FDA from utilizing any funds to propose or otherwise promulgate any rule that requires or permits any prescription drug or biologic products to be distributed without printed prescribing information on or within the packaging from which such products are to be dispensed, unless such actions are expressly provided by an amendment to the FDCA.

FDA Response:

On December 18, 2014, FDA published a proposed rule that would provide for electronic distribution of prescribing information (professional labeling) for human prescription drugs and biological products. Pursuant to Section 746 of the Omnibus Spending Bill of December 18, 2015 (Pub. Law No. 114-113), the Agency stopped work on finalizing the proposed rule. In FDA's view, if finalized, the rule would have modernized the system for disseminating drug information and utilized available technological advancements. Such advancements would make it possible for healthcare providers to access new safety information about the drugs and biological products they are prescribing and dispensing much quicker than the current system, thereby enabling them to make decisions about patient care based on the most up-to-date information possible. Also, the above-referenced GAO report addressed both professional and patient labeling. However, the proposed rule pertained only to professional labeling for prescription drugs — it did not propose any changes to the distribution of patient labeling for prescription drugs.

Additionally, under the proposed rule, FDA on its own initiative or upon request from a manufacturer can exempt a product from the electronic distribution requirements if compliance could adversely affect the safety, effectiveness, purity or potency of the drug, is not technologically feasible, or is otherwise inappropriate. The rule also proposed to require drug manufacturers to provide labeling in paper format to any patient or provider upon request.

45. President's Budget Submission to Congress

The Administration has submitted the President's budget request the past two years with a false level of base funding for the agency. Congress provided funds for the Department of Health and Human Services OIG in the FDA's Salaries and Expenses Appropriation in fiscal years 2015 and 2016. While those funds were transferred to the OIG following an apportionment by the Office of Management and Budget, such a transfer did not alter the Congressional appropriation level for the FDA. The Subcommittee directs the FDA to incorporate the actual funding level approved by Congress when displaying the previous year funding level in the fiscal year 2018 President's budget.

FDA Response:

FDA will incorporate the actual funding level approved by Congress when displaying the previous year funding level in the fiscal year 2018 President's budget.

46. Private Accredited Laboratories

As the FDA begins to implement the regulations associated with FSMA and increase sampling of food products, the agency is encouraged to use and contract with, when appropriate, ISO/IEC 17025 certified, and other certified laboratories to advance the goals of FSMA and for other data collection purposes.

FDA Response:

FDA agrees with the importance of obtaining analyses from laboratories using reliable quality management systems. To that end, the FDA Foods and Veterinary Medicine Program will use

laboratories accredited under ISO/IEC 17025 and other certified laboratories, as appropriate, for sample collection and analysis.

47. Protecting Proprietary Information

The Committee is concerned about the FDA's ability to protect trade secrets and confidential information the agency obtains from its regulated industries. FDA's access to such information has been expanded under FSMA and other regulatory actions. Recent cybersecurity breaches at the FDA underscore the importance of the FDA's ability to safeguard sensitive information. The agency has a legal obligation under the FDCA to protect confidential information. The Committee directs the FDA to provide a detailed plan on how this information will be protected no later than 60 days after enactment.

FDA Response:

Information security is among the top priorities at the FDA, and we do not take lightly our responsibility for protecting industry and public health information in today's environment of increased cybersecurity risk. The agency recognizes the risks associated with operating this large global IT enterprise and has implemented processes, procedures, and tools to better ensure the prevention, detection and correction of incidents. Since October 2013, FDA is not aware of any recent cybersecurity breaches at the agency. FDA will provide the requested report.

48. Public Disclosure

The FDA's current rules and policies governing what drug and device developers may say about their own products were designed decades ago. Since then, the way that medicine is practiced and delivered and the way that information is communicated have fundamentally changed. The Committee urges the FDA to convene a working group with stakeholders, including representatives from government, industry, health professionals, and patient advocacy groups, in order to solicit information to inform the FDA's evaluation of its rules and policies regarding the appropriate scope of scientific and medical information that can be shared with physicians, insurers, and researchers, with appropriate safeguards, in order to optimize patient care.

FDA Response:

FDA is committed to continuing a robust dialogue regarding scientific and medical information. In furtherance of the commitment the agency in recent years has convened public meetings, opened dockets and issued new guidance. The agency will continue to encourage appropriate discussions and will consider approaches that may further that aim.

49. Ready-to-Eat Foods

The Committee is aware that the FDA is in the process of finalizing guidance documents regarding *Listeria monocytogenes* in ready-to-eat (RTE) foods, which may include frozen vegetables that are not currently considered as RTE foods. Reducing incidents of listeriosis is an important health goal, and the Committee supports the issuance of scientifically based guidance. However, including foods that are not considered RTE should be justified based upon a quantitative risk assessment. The Committee urges the FDA to conduct such an assessment prior

to taking any action that would formally consider frozen vegetables or other foods currently not considered RTE as RTE foods.

FDA Response:

FDA determines the risk associated with *Listeria monocytogenes* in a frozen food, such as a frozen vegetable, on a case-by-case basis depending on a number of factors, including whether it supports the growth of the pathogen when thawed and how the frozen food is commonly handled. Some frozen vegetables present minimal risk to consumers because these vegetables are commonly held frozen, cooked from a frozen state, and immediately consumed. By contrast, some frozen vegetables can be thawed and used without cooking in salads, whether in commercial salad bars or in the home; and some recipes available to consumers describe the preparation of products using frozen vegetables that are thawed, but not cooked. Where a frozen food that supports growth of *L. monocytogenes* is thawed and held for considerable time at refrigerated or room temperature, such as on a salad bar, it may pose a risk to consumers because it has not been subject to cooking that would kill the pathogen and it will be held under conditions that allow pathogen growth to occur.

Every few years, FDA identifies new vehicles for *L. monocytogenes* illness among foods with no known prior history of contamination or epidemiological link to listeriosis, and some foods with limited histories of contamination can prove to be higher risk than previously thought. For example, in 2016, CDC identified a multistate outbreak of listeriosis linked to frozen vegetables by epidemiologic and laboratory evidence. We anticipate that the pattern of discovering new food vehicles will continue, if not hasten, with the advancement of whole genome sequencing in connecting known clinical illnesses with the foods responsible for those illnesses.

The Committee's request for an assessment, prior to any other action, would hinder the Agency's efforts to prevent public health problems involving *L. monocytogenes*-contaminated frozen vegetables. Moreover, this would be a costly undertaking because the type of comprehensive up-to-date survey data needed to develop a quantitative risk assessment for foodborne *L. monocytogenes* in frozen vegetables is not presently available; therefore, FDA would have to conduct its own survey prior to conducting such a risk assessment or commission another organization to conduct such an assessment. For example, a 2003 Quantitative Assessment of Relative Risk to Public Health from Foodborne *Listeria monocytogenes* Among Selected Categories of Ready-to-Eat Foods -- jointly developed by FDA, the Centers for Disease Control and Prevention, and the USDA's Food Safety and Inspection Service -- took four (4) years to complete, beginning with a *Federal Register* notice of intent issued in 1999 and culminating in completion of the final assessment in 2003. Given current consumer and retailer practices for using some kinds of thawed, uncooked frozen vegetables without cooking, FDA believes we can scarcely afford this delay.

50. Scientific Integrity

Pursuant to the President's 2009 memorandum and as directed by the Office of Science and Technology Policy, the FDA adopted a scientific integrity policy in 2012. It appears to conform to the President's directive by maintaining a firm commitment to science-based, data-driven decision making, facilitating the free flow of scientific and technical information, and requiring a fair and transparent approach to resolving scientific disputes. The Committee directs the

Commissioner to ensure all FDA centers agencies are complying with the policy and using it to guide their policy and regulatory decisions.

FDA Response:

FDA's policies related to scientific integrity currently apply to all Agency components and employees. The Office of Scientific Integrity within the Office of the Commissioner is regularly working with the Agency's centers and other components to ensure compliance with these policies and encourages employees to report deviations from them.

51. Sodium Guidance

The Committee is aware that the FDA is considering issuing guidance to food manufacturers in order to reduce sodium in various food categories. It is imperative that any guidance be issued using the latest sound science. The Centers for Disease Control and Prevention and the IOM are working together to update the Dietary Reference Intake (DRI) report on sodium. The FDA is encouraged to issue any voluntary or mandatory guidance based upon an updated DRI report.

FDA Response:

In June 2016, FDA issued draft guidance for public comment for voluntary sodium reduction goals in commercially processed and prepared food, both in the short-term and over the long-term (81 FR 35363). This draft guidance was based on the latest scientific evidence available, and reflects recommendations in the most recent Dietary Reference Intakes (DRI)¹⁰⁵ for sodium, as well as the recently issued 2015-2020 *Dietary Guidelines for Americans* (which involved expert review of the current body of research by the Dietary Guidelines Advisory Committee). FDA's draft voluntary short-term (two-year) targets are aimed at reducing average sodium consumption from 3,400 to 3,000 mg/day, and the voluntary long-term (ten-year) targets are aimed at reducing average sodium consumption to 2,300 mg/day, which is consistent with current federal recommendations. FDA also strongly supports efforts by the National Academies of Science, Engineering and Medicine (National Academies) to formally review the sodium DRI, and FDA is collaborating with CDC, NIH, and USDA to update the DRI for sodium as expeditiously as possible.

The majority of Americans are trying to take action to reduce their sodium intake (CDC, 2015), and the weight of the scientific evidence supports reducing sodium in the food supply in order to reduce current average sodium consumption levels from 3,400 mg/day—well above the current recommended limit of 2,300 mg/day—, thereby reducing the risks associated with increased blood pressure and cardiovascular disease (CVD). Three quarters of sodium intake comes from processed or prepared food – before it is added at the table, or during cooking. Supporting options for food products lower in sodium therefore increases choices for American consumers. Several major food manufacturers are supportive of FDA's efforts in their recently submitted comments on the draft voluntary sodium reduction targets.

Given the scientific evidence in support of reducing sodium intake from current levels to reduce blood pressure, subsequent CVD, and associated health care costs, as well as recent industry

¹⁰⁵ The Dietary Reference Intakes (DRIs) are nutrient reference values developed by the Institute of Medicine of The National Academies of Sciences, Engineering, and Medicine.

feedback on the targets, the Agency believes that it is reasonable to continue work on voluntary sodium reduction targets, even as the DRI is updated. Once the DRI report is finalized (anticipated to be in 2019), FDA is committed to making any needed adjustments to the long-term targets to align them with the findings of the National Academies Committee. Furthermore, FDA will continue extensive outreach with industry and public health groups on our draft voluntary targets to ensure that they are well understood.

52. Spent Grains

The Committee recognizes that the FDA took into consideration public comments and revised some of its proposed regulations on spent grains used for animal food. Processors already complying with FDA human food safety requirements would not need to implement additional preventive controls when supplying a by-product like wet spent grains for animal food. However, further processing a by-product for use as animal food such as drying spent grains, would require additional compliance under the proposed rule. The FDA has said that potential hazards associated with spent grains are minimal and steps to prevent contamination are likely already in place. The Committee includes bill language to ensure dry and wet spent grains used for animal food are regulated equally.

FDA Response:

Americans purchasing human and animal food expect that the food is safe and not adulterated, and produced in a manner that protects it from contamination. There are two general types of spent grains of the alcoholic beverage production process that are used as animal food: unprocessed spent grains (“wet spent grains”) and processed spent grains (“dried spent grains”). During a recent education and outreach event with the alcoholic beverage manufacturing industry, we learned that for certain segments of the industry there are “intermediary by-products” produced in addition to spent grains that also are used as animal food. The by-product that is more processed (i.e., dried spent grains) may be more likely to be contaminated because additional processing of the by-product allows more opportunities for the introduction of contamination.

In the Current Good Manufacturing Practice, Hazard Analysis, and Risk-Based Preventive Controls for Food for Animals final rule (PCAF rule), FDA established two major sets of new requirements for animal food. FDA established current good manufacturing practice (CGMP) requirements for animal food under section 402 of the FD&C Act to help ensure animal food is manufactured in a manner that protects it from contamination. The PCAF rule also established the hazard analysis and risk-based preventive controls requirements as required by FSMA.

CGMPs are baseline manufacturing standards to protect food against contamination. Alcoholic beverage manufacturing facilities are subject to human food CGMPs for the production of their alcoholic beverages and animal food CGMPs for spent grains for use as animal food. The animal food CGMPs are similar to the human food CGMPs, but include more flexibility for implementation than the human food CGMPs. FDA understands the Committee's concern with respect to the hazard analysis and preventive control requirements of the PCAF rule and does not intend to apply these requirements to alcoholic beverage manufacturers processing spent grains for use as animal food.

As discussed in our education and outreach meetings with the alcoholic beverage industry, FDA wants to ensure all by-products of the alcoholic beverage industry remain subject to the baseline CGMP requirements that protect against contamination of animal food that result in adulteration under the FD&C Act. We will continue to convey this message in further outreach and education efforts to the alcoholic beverage industry.

FDA will use the information gained through our continued outreach with the industry to develop both training material and guidance for our field staffs. Regulators and industry share a common goal of achieving compliance while maintaining standards for food safety and public health.

FDA believes it can achieve this common goal of safe animal food through education and outreach and through the implementation of the CGMPs at these facilities.

53. State Inspections

The Committee is aware of the December 2011 OIG report that outlined vulnerabilities in the agency's oversight of non-FDA food inspections and the agency's intention to further rely on state inspections. The Committee understands that both the federal government and states share authority and responsibility for domestic food facilities and that the FDA will continue to contract with the states to conduct inspections on its behalf, which is critical to performing its mission in an efficient and effective manner. The agency must assure it has strong federal inspection standards that are met by both federal investigators and state inspectors. The FDA must continue its progress in improving federal oversight and monitoring of state inspection programs, reviewing and strengthening internal directives and processes, and identifying new methods to improve oversight capabilities.

The FDA should continue working with states to: (1) build the capacity and effectiveness of their inspection programs through implementation of national program standards, such as the Manufactured Food Regulatory Program Standards and the Animal Feed Regulatory Program Standards; (2) utilize state or private laboratory services with ISO/IEC 17025 laboratory accreditation; and (3) improve federal-state collaboration during investigations and responses to food borne illness outbreaks by supporting the implementation of Rapid Response Teams.

The Committee is aware of the FDA's continuing progress to modernize existing IT systems and infrastructure, allowing for the secure and efficient exchange of data between the FDA and the states, in addition to efforts to add capabilities supporting mobile inspection applications. The FDA should continue work with state partners toward promoting data standards and developing shared database schemas to facilitate secure electronic information sharing.

FDA Response:

FDA did a great deal of work following the 2011 OIG study. Significant resources have been allocated to evaluating the study findings, internal processes and procedures and enhancing FDA operations. FDA is continuing to audit state regulatory programs and implement a quality review of state inspections conducted under contract. FDA also continues to improve federal-state work planning communication, coordination and collaboration to leverage resources and

improve efficiency and effectiveness in the prevention of human and animal food contamination and illness.

FDA is continuing to improve its regulatory program standards in collaboration with state partners and to provide training and resources to states as well as FDA investigators to ensure all investigators and inspectors have the knowledge, skills and abilities to competently inspect, conduct investigations, gather evidence, collect samples and take enforcement actions. FDA district offices continue to review state-conducted inspection assignments in accordance with the contract statement of work requirements. Both FDA and state regulatory agencies continue to execute audits of the contract inspection programs in accordance with the FMD-76 audit requirements.

The Agency has collaborated with our state regulatory partners to review, modify and enhance the MFRPS and released an updated version of the standards in 2016. Additionally, a collaborative review of both the MFRPS and the AFRPS is currently underway as part of the three-year review cycle. FDA and the states will work jointly to enhance both programs where possible. FDA continues to provide financial support and technical assistance to states for the implementation of the national program standards, including the MFRPS, AFRPS, and Voluntary National Retail Regulatory Program Standards. We continue to see enhanced participation from the states in the MFRPS program as well as the AFRPS program. In addition, we are collaborating with states to develop new standards for egg and shellfish regulatory programs.

Both FDA and the states continue to leverage resources and abilities through the use of Rapid Response Teams (RRTs), which are utilized when dealing with food outbreaks/emergencies. State and FDA counterparts continue to train together and FDA continues to devote financial and human resources to support, develop and implement RRTs. Both the states and FDA remain invested in RRTs and the continued use and progression of this collaborative resource.

FDA continues to improve its IT capabilities, working with our state partners to enhance existing IT systems that allow for the transmission of information between the Agency and states. FDA is also evaluating other existing Agency IT systems to determine their viability for use in state communications. In FY17, FDA is establishing an Initial Operating Capability (IOC) for a National Food Safety Data Exchange (NFSDX) platform to conduct a pilot automated electronic sharing of contracted inspection data with a few partner states. As of April 1, 2017, seven states have signed up to participate in the NFSDX pilot testing scheduled for July and August. By September 2017, a plan for a Full Operating Capability (FOC) will be completed to prepare for extending beyond the pilot states to the other partner states in the near future. FDA will continue to work with our state partners to enhance and further the IT infrastructure to advance new mechanisms to allow for the secure and efficient exchange of data between FDA and the states.

54. Staffing at Land Ports of Entry

The Committee is concerned that USDA, FDA, and Customs and Border Protection are relying on historical data in determining their staffing models at Land Ports of Entry. Recent reports on agriculture imports show steep increases in the future, especially along the Southwest border and South Texas in particular. It is the sense of the Committee that these agencies should be utilizing forward looking data for their staffing models to ensure we have an appropriate workforce available in the future to inspect and certify this growth in agriculture imports as efficiently, safely and expeditiously as possible.

FDA Response:

FDA's electronic import processing systems allow the Agency to review import entries without having to physically be at the actual port of entry. These systems interface with CBP's Automated Commercial Environment (ACE) system. FDA's import entry screening tool (PREDICT) calculates a customized risk score based on a wider variety of factors, including, but not limited to, inherent risk of the product, data anomalies, data quality, and the compliance history of firms (e.g., manufacturer, shipper, and consignee) and the product; to get the best use of FDA's limited resources, staffing decisions should assess not only the volume of products entering through a particular port of entry, but also the overall risk of those products compared to other ports of entry.

FDA is developing new system-based, import-centric processes under FSMA, such as the Foreign Supplier Verification Program (FSVP) regulation and the Voluntary Qualified Importer Program (VQIP), that are risk-based and are less reliant on an increased level of surveillance or end product testing. The FSVP regulation requires that importers perform certain risk-based activities to verify that food imported into the United States has been produced in a manner that meets applicable U.S. safety standards. In addition, VQIP will provide for the expedited review and importation of foods from importers who achieve and maintain a high level of control over the safety and security of their supply chains. These programs represent a better use of FDA resources than placing staff at ports of entry without consideration of product risk.

FDA tries to staff ports of entry based on volume and risk associated with the products imported through those ports, in line with the resources available. Adding physical coverage to specific ports of entry without adding additional resources means decreasing capacity in other ports of entry. Additionally, relocating staff from one port to another raises retention and union issues which must be considered.

55. Sunscreen Ingredients

The Committee is significantly concerned that despite the increase in incidence of skin cancer 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 President Obama's January 2016 Presidential Memorandum creating the White House Cancer Moonshot Task Force to prevent and cure cancer, the FDA has still not approved a new OTC sunscreen ingredient through the process created by the SIA. For several years, the House and Senate Appropriations Committees have directed the FDA to clear the sunscreen backlog and ensure that Americans have access to the latest skin cancer prevention technology (H. Rept. 113-116, H. Rept. 113-468, H. Rept. 114-205, S. Rept. 114-82). The agency has failed to do so. The Committee directs the FDA to work with stakeholders to develop a benefit-risk testing regimen that appropriately balances the benefit of additional skin cancer prevention tools versus the risk of skin cancer to the 5 million Americans that will be diagnosed with the condition this year. The agency is directed to reach agreement with stakeholders on this testing regimen by June 20, 2016 and publish the summary of the meetings and results of the specific testing requirements on its website. The Committee reminds the FDA that section 4(c) of the SIA requires the FDA to report to the Senate Health, Education, Labor and Pensions Committee and House Energy & Commerce Committee on the implementation of the Act on or before May 26, 2016. The FDA shall include in this report a detailed analysis of how the FDA is balancing the Surgeon General's Call to Action, the

President's Moonshot effort to remove administrative hurdles to cancer prevention, the known public health benefits that regular sunscreen use provides to prevent skin cancer and melanoma, and the long history of safe and effective use of sunscreens currently backlogged at the FDA in comparable countries versus the hypothetical risk sunscreens theoretically may pose to human health in FDA's GRAS standard. The funding level for the FDA maintains the \$700,000 increase in Fiscal Year 2016 to help address the critical public health threat resulting from no new sunscreen ingredients being available to the public.

FDA Response:

FDA transmitted the report entitled "Report in Response to Sunscreen Innovation Act (P.L. 113-195) Section 586G" to the Committee on Energy and Commerce on May 23, 2016.

FDA has carefully considered what information is needed to ensure that a particular sunscreen active ingredient is safe and effective for use in OTC sunscreen products. FDA's recommended studies reflect the Agency's scientific expertise, existing technical guidance, experience from reviewing safety and efficacy data submitted for a generally recognized as safe and effective (GRASE) review of sunscreen active ingredients seeking to be added to the OTC Review for Sunscreens under current OTC drug regulations, and input from outside scientific experts (<http://www.fda.gov/AdvisoryCommittees/Calendar/ucm407137.htm>). The recommended studies are not novel and are consistent with FDA's standard data requirements for both nonprescription and prescription topical drugs intended for chronic use.

Information on FDA's recommendations and expectations for the safety data needed to show that an active ingredient is GRASE for use in nonprescription sunscreen products has been publicly shared with industry and other interested parties on multiple occasions, including a public advisory committee meeting held in September 2014, proposed sunscreen orders published in 2014 and early 2015 for the eight sunscreen active ingredients that were under evaluation by FDA when the SIA was enacted, sponsor-requested meetings on the proposed sunscreen orders, and an SIA-required draft guidance for industry published in November 2015, which the FDA finalized in November, 2016.

To date FDA has met all statutorily mandated SIA deadlines and remains committed to achieving that goal in the future.

56. Surrogate Endpoints

The Committee urges the FDA to issue guidance on the use of surrogate and intermediate endpoints for accelerated approval of regenerative medicine products under section 506(c) of the FDCA (21 U.S.C. 356(c)). In the process of issuing guidance, the FDA shall consult with appropriate stakeholders in the development of this guidance.

FDA Response:

The FDA's Center for Biologics Evaluation and Research is committed to helping make regenerative medicine therapies that are shown to be safe and effective available as soon as possible. FDA has an Expedited Programs guidance that addresses the use of surrogate and intermediate endpoints for accelerated approval; this guidance applies to regenerative medicine

therapies that are drugs and biologics and that meet the criteria for accelerated approval (Expedited Programs for Serious Conditions – Drugs and Biologics, published in May 2014).

Building on the FDA’s existing expedited programs available to regenerative medicine products, the Regenerative Medicine Advanced Therapy (RMAT) Designation was established through the 21st Century Cures Act, signed into law in December 2016. Drugs that are regenerative medicine therapies, as defined in the new law, may obtain the RMAT designation if the drug is intended to treat, modify, reverse, or cure a serious or life-threatening disease or condition and if there is preliminary clinical evidence indicating that the drug has the potential to address unmet medical needs for that disease or condition.

RMAT-designated products are eligible for increased interactions with the FDA, similar to those interactions available to sponsors of breakthrough-designated therapies. In addition, they may be eligible for priority review and accelerated approval. The legislation recognizes that these early meetings between FDA and sponsors of RMAT-designated products may be a suitable time to discuss whether accelerated approval would be appropriate based on surrogate or intermediate endpoints reasonably likely to predict long-term clinical benefit, or reliance upon data obtained from a meaningful number of sites. FDA is committed to continuing to advance the development of drugs and biological products, including by providing more guidance related to surrogate endpoints and implementing the drug development tools provisions of the 21st Century Cures Act, and will continue to engage sponsors and other stakeholders on this issue.

57. User Fee Collections/Obligations

The Committee continues to be concerned about the financial management of the FDA’s user fee programs. The Committee directs that not later than 30 days after enactment of this Act, and each month thereafter through the months covered by this Act, the Commissioner to submit to the Committees on Appropriations of the House and Senate a report on user fees collected for each user fee program included in the Act. The report shall also include monthly obligations incurred against such fee collections. The report shall include a distinct categorization of the user fee balances that are being carried forward into fiscal year 2018 for each user fee account as well as a detailed explanation of what accounts for the balance and what the balance will be used for.

FDA Response:

FDA will provide the requested reports.

58. Funding for Food Safety

Funding for Food Safety.--The Committee includes increases of \$33,152,000 for the implementation of FSMA. These increases include \$19,139,000 for the National Integrated Food Safety System (NIFSS) and \$14,013,000 for Import Safety. The increases provided in this bill and the increases provided since fiscal year 2011 should assist the FDA in preparation for the implementation of FSMA prior to the effective dates of the seven foundational proposed rules. While the FDA has not implemented the final rules, the Committee understands that most businesses will not need to comply with the two rules for preventive controls for human food and for animal food until August 2016 and that the other five rules will not be effective until fiscal

year 2017 and later. Within the amount provided for NIFSS, the Committee includes \$5,000,000 to allow for the development of a data exchange to maximize standardization and access to farm data across FDA and States.

FDA Response:

FDA will provide a response to Congress for this Significant Item in a supplemental package.