HOUSE APPROPRIATIONS COMMITTEES SIGNIFICANT ITEMS

HOUSE COMMITTEE REPORT (114-205)

1. Active Pharmaceutical Ingredients

The Committee is concerned that the FDA has not yet approved a list of Active Pharmaceutical Ingredients (APIs) for use by compounding pharmacists pursuant to the Drug Quality and Security Act (Public Law 112-43, 127 Stat. 587) and the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 353a et seq.). Within 90 days of enactment of this Act, the FDA shall report to Congress on when its review of proposed APIs pursuant to § 503A(1)(a)(iii) will be completed.

FDA Response:
FDA will provide the requested report.

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 A draft Guidance for Industry document on possible streamlined drug development pathways for drugs with the capacity to be used for the treatment of serious bacterial diseases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. Cooperation between FDA and industry, along with our partners in other Public Health Service agencies, could facilitate advancements in the field, providing a robust clinical and pre-clinical network to develop and improve new antibacterial therapies. These initiatives may advance the quality and efficiency of clinical trials, while facilitating innovation in drug development.

3. Bioethics

The Committee notes that the FDA commissioned a consensus study from the Institute of Medicine (IOM) on "Ethical and Social Policy Considerations of Novel Techniques for Prevention of Maternal Transmission of Mitochondrial DNA Diseases." The Committee further notes that the FDA has requested that the IOM produce a consensus report on the ethical and social policy issues related to genetic modification of eggs and zygotes to prevent transmission of mitochondrial disease. The Committee directs the FDA to establish an independent panel of experts, including those from faith-based institutions with expertise on bioethics and faith-based medical associations, and to submit this consensus report to the independent panel of experts upon its completion by the IOM. The Committee urges the independent panel of experts to review the IOM report and report their evaluation of its conclusions, along with any

recommendations based on this review, to the Committee within 30 days of the completion of the report by the IOM.

FDA Response:
FDA has commissioned the Institute of Medicine (IOM) to conduct a consensus study to develop a report that will inform FDA in consideration of review of applications in the area of genetic modification of eggs and zygotes for the prevention of mitochondrial disease. The development of novel techniques in this area raises complex ethical and social policy issues, thus, FDA has tasked the IOM to address a broad range of issues including the foundational question of whether safeguards such as specific measures and public oversight could adequately address the social and ethical concerns, or whether those concerns preclude clinical trials.

Specifically, the IOM committee developing the report includes members with expertise in religious studies, bioethics, health policy, legal matters, mitochondrial science, reproductive medicine, and medical history, as well as a patient representative. Therefore, FDA believes the IOM consensus study adequately takes into consideration the position of faith-based institutions. The IOM consensus study will also address a broad range of ethical and social policy issues. Additionally, to develop the report, the IOM committee has held several meetings and workshops, and will convene several more times. The workshop held in late March 2015 included presentations from and discussions with experts from faith-based institutions with expertise on bioethics, including faith-based medical associations.

4. 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. Please be aware that the comment period on the draft guidances, concerning repackaging of certain human drug products and concerning mixing, diluting, and repackaging biological products by state-licensed pharmacies, Federal facilities, and outsourcing facilities closed on May 20, 2015. FDA received over 300 comments on the draft guidance concerning mixing, diluting, and repackaging biological products by state-licensed pharmacies, Federal facilities, and outsourcing facilities, and over 600 comments on the draft guidance concerning repackaging of human drug products. FDA intends to review the comments and finalize both guidance documents as quickly as it can.

5. Blood Plasma Products

The Committee notes that the FDA has followed the Committee's advice from fiscal year 2015 and is addressing the issue of the use of plasma for post-collection manufacture into critical plasma derivatives, no matter the manner in which the blood is collected. The Committee urges the FDA to prioritize developing policies to allow for the more timely use of plasma from

automated donations into other biologics and asks that the FDA update the Committee on its progress with a report no later than 60 days after enactment of this Act.

FDA Response:
FDA will provide the requested report.

6. Blood Product Policies

Last December, the FDA released draft guidance for industry entitled "Bacterial Detection Testing by Blood Collection Establishments and Transfusion Services to Enhance the Safety and Availability of Platelets for Transfusion." As the agency is aware, the Committee issued report language in fiscal year 2012 expressing concern for the safety risks to transfusion patients from bacterially contaminated platelets. The Committee is pleased to see the agency take the step of releasing draft guidance. Unfortunately, when the FDA released its guidance agenda for 2015, the final version of this draft guidance was not listed among the agency's priorities. This is an important safety issue, and it is essential that the agency complete the guidance process in a timely manner. The Committee urges the FDA to do so as quickly as possible.

FDA Response:
FDA issued draft guidance in December 2014, "Bacterial Detection Testing by Blood Collection Establishments and Transfusion Services to Enhance the Safety and Availability of Platelets for Transfusion; Draft Guidance for Industry". Taking into account public comments and the recent approval of a pathogen reduction technology for a widely used method of preparing platelets, FDA intends to issue a revised draft guidance for comment before finalizing the guidance. In May 2015, FDA published a final rule Requirements for Blood and Blood Components Intended for Transfusion or for Further Manufacturing Use (80 FR 29842)**.** This final rule "requires establishments to have procedures to control the risks of bacterial contamination of platelets" (21 CFR 606.145). The final rule becomes effective in May 2016. The FDA's revised draft guidance will provide recommendations for complying with this regulatory requirement.

7. Cord Blood Regulation

The Committee directs the FDA to undergo a review and seriously consider the potential need for revision of the current regulatory requirements for cord blood licensure, particularly those related to manufacturing and storage, to ensure the correct applicability to this industry since the current regulatory requirements are the same ones that apply to pharmaceutical products. In addition, the Committee directs the FDA to create an advisory task force, comprised at a minimum of public and private cord blood bankers, transplanters and patients, to provide recommendations to the agency about the current licensing requirements and changes that may be necessary.

FDA Response:
FDA developed an innovative regulatory paradigm for minimally manipulated, unrelated allogeneic placental/umbilical cord blood (HPC, Cord Blood) through extensive outreach and collaboration with our stakeholders. This regulatory program has resulted in HPC, Cord Blood units that are manufactured more consistently without interfering with product availability.

The manufacturing and storage requirements, as well as other requirements, were developed in collaboration with our stakeholders through various means including: two meetings of the Cellular, Tissue, and Gene Therapy Advisory Committee; development of the final guidance, ''Class II Special Controls Guidance Document: Cord Blood Processing System and Storage Container;" two rounds of guidance development regarding recommendations for IND and

Biologics License Application submissions for HPC, Cord Blood; a cord blood licensure workshop; outreach to the Health Resources Services and Administration (HRSA); outreach to the National Marrow Donor Program (NMDP); outreach at professional meetings; more than 10 pre-BLA meetings with stakeholders; and through participation as a liaison to the HHS Advisory Council on Blood Stem Cell Transplantation (ACBSCT).

The ACBSCT advises the Secretary of HHS and the Administrator of HRSA on the activities of the C.W. Bill Young Cell Transplantation Program and the National Cord Blood Inventory (NCBI) Program. Members of the ACBSCT include representatives of marrow donor centers, transplant centers, and cord blood banks, patient and patient family representatives, scientists, ethicists, and members of the general public.

In addition, FDA has met recently with the NMDP and representatives of licensed cord blood banks to discuss lessons learned and identify ways in which FDA and the industry may work together to facilitate further development of HPC, Cord Blood products. Based on the input obtained, the manufacturing and storage requirements are considered appropriate for HPC, Cord Blood licensure, and FDA is committed to working with industry to improve best practices under the current regulations.

8. Cosmetics and Colors

The Committee directs the FDA to spend no less than the fiscal year 2015 level for cosmetics activities as well as for the Office of Colors and Cosmetics (OCAC). Funding provided for OCAC is for direct support of the operation, staffing, compliance, research, and international activities performed by this office. The Committee notes that, for the past five years, it has directed the FDA to respond to the Citizen Petition requesting that the FDA establish a safe level for lead as a nonfunctional constituent in lipstick. The Committee is aware that in 1975 the cosmetic industry asked the FDA to evaluate the safety of ingredients found in its products. Consistent with this commitment, in 1976 the cosmetic industry established the Cosmetic Ingredient Review (CIR) under which the safety of approximately 3,880 ingredients has been reviewed by an Expert Panel of independent scientists, and the FDA has participated through a nonvoting liaison at all meetings of the Expert Panel. The Committee directs the FDA to respond to the Citizen Petition on this lipstick ingredient by December 31, 2015.

FDA Response:
OCAC will use FY 2016 funding for direct support of the operation, staffing, compliance, research, and international activities performed by this office. As noted in our response to the Committee last year, FDA sponsored and completed additional studies to address data gaps regarding trace amounts of lead in cosmetic products. FDA has evaluated data from these studies and other relevant information and has worked to respond fully to the citizen petition.

9. Cosmetic Ingredient Review Panel

As noted, the cosmetic industry established the CIR as a means to assure the safety of ingredients in cosmetic products. Given the breadth and volume of ingredients reviewed and the scientific expertise applied to its process, it is the Committee's belief CIR should be recognized and formalized as a public-private program. The Committee therefore directs that the FDA work with the cosmetic industry to transfer the CIR to the United States Pharmacopeia Convention (USP) or some other appropriate third body for the purpose of evaluating and determining the safety of ingredients found in cosmetics. USP is a widely respected independent scientific organization whose drug standards are explicitly incorporated under the Federal Food, Drug, and

Cosmetic Act (FDCA). The Committee directs that the FDA, working cooperatively with the cosmetic industry, report back to the Committee no later than January 15, 2016, with a framework and a detailed plan.

FDA Response:
While FDA will prepare the requested report, the Committee's directive raises significant appearance concerns and resource issues that will be addressed in the report. The CIR is a private, industry-funded organization, and FDA believes that enhancing the authority and stature of a private organization is inappropriate for a Federal regulatory agency. In addition, charging a public-private partnership with determining the safety of cosmetic ingredients – an activity within the Agency's statutory purview – may create the appearance that the partnership's determinations represent formal FDA determinations.

10. Drug Compounding

The Committee is concerned that, since passage of the Drug Quality and Security Act (DQSA) of 2013, FDA has interpreted provisions of Section 503A of the FDCA in a manner inconsistent with its legislative intent and with the agency's own previous positions. Specifically, the FDA has taken the position that under 503A, a pharmacist may not compound medications prior to receipt of a prescription and transfer the drugs to a requesting physician or other authorized agent of the prescriber for administration to his or her patients without a patient-specific prescription accompanying the medication. This practice, which is often referred to as "office-use" compounding, is authorized in the vast majority of states and was intended to be allowable under DQSA. The Committee is aware that in 2012, prior to passage of the DQSA, FDA was working on a draft compliance policy guide for 503A of the FDCA that provided guidance on how "office-use" compounding could be done consistent with the provisions of 503A. The Committee understands the intent of the DQSA was not to prohibit compounding pharmacists from operation under existing 503A exemptions; therefore, the Committee directs the FDA to issue a guidance document on how compounding pharmacists can continue to engage in "office-use" compounding before the receipt of a patient-specific prescription consistent with the provisions of 503A within 90 days after the enactment of this Act.

FDA Response:
FDA is considering the report language concerning office use in FY 2015 House Report 114-205. FDA recognizes that sometimes it is necessary for health care practitioners in hospitals, clinics, offices, or other settings to have certain compounded drug products on hand that they can administer to a patient who presents with an immediate need for the compounded drug product. For example, if a patient presents at an ophthalmologist's office with a fungal eye infection, timely administration of a compounded antifungal medication may be critical to preventing vision loss.

In such a case, the prescriber may need to inject the patient with a compounded drug product immediately, rather than writing a prescription and waiting for the drug product to be compounded and shipped to the prescriber. In other cases, compounded drug products may need to be administered by a health care practitioner in his or her office because it would not be safe for the patient to take the drug home for self-administration, and it would not be practical for the patient to bring a prescription for the compounded drug product to a pharmacy and then return to the health care practitioner for administration.

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, licensed pharmacists and licensed physicians who compound drug products in accordance with section 503A are not required to comply with current good manufacturing practice (CGMP) requirements.

Furthermore, FDA does not interact with the vast majority of licensed pharmacists and licensed physicians who compound drug products and seek to qualify for the exemptions under section 503A of the FD&C Act for the drug products they compound because these compounders are not licensed by FDA and generally do not register their compounding facilities with FDA. Therefore, 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.

In 2012, contaminated injectable drug products that a compounding pharmacy shipped to patients and health care practitioners across the country caused a fungal meningitis outbreak that resulted in more than 60 deaths and 750 cases of infection. This outbreak was the most serious of a long history of outbreaks associated with contaminated compounded drugs. Since the 2012 fungal meningitis outbreak, FDA has investigated numerous other outbreaks and other serious adverse events, including deaths, associated with compounded drugs that were contaminated or otherwise compounded improperly.

FDA has also identified many pharmacies that compounded drug products under insanitary conditions whereby the drug products may have been contaminated with filth or rendered injurious to health, and that shipped the compounded drug products made under these conditions to patients and health care providers across the country, sometimes in large amounts. The longer a compounded sterile drug product that has been contaminated is held by a pharmacist or physician before distribution, or held in inventory in a health care facility before administration, the greater the likelihood of microbial proliferation and increased patient harm. Because of these and other risks, the FD&C Act places conditions on compounding that must be met for compounded drugs to qualify for the exemptions in section 503A.

In establishing policies on office use, FDA intends to consider important public health issues, including the need for access to products for office use and the need to protect patients from poor quality compounded products, as well as the statutory language in section 503A of the Federal Food, Drug, and Cosmetic Act, the category of outsourcing facilities created by new section 503B of the Act, and the need to provide a clear line between permissible compounding and impermissible manufacture of unapproved drugs.

11. Drug Labeling Approval

The Committee acknowledges FDA's actions over the past six months regarding the proposed rule, "Supplemental Applications Proposing Labeling Changes for Approved Drugs and Biological Products," to include a listening session on March 27, 2015, and a reopened comment period that closed on April 27, 2015. However, the Committee continues to be concerned with FDA actions from the beginning of this process and the subsequent failure to find closure on this issue. As things currently stand, the rule would allow a generic drug manufacturer to alter its safety labeling unilaterally without FDA's prior approval, even if there is more than one generic manufacturer or an innovator manufacturer and generic manufacturer marketing the same bioequivalent drug (a "multisource" drug), and other companies are not required to make a

corresponding labeling change. p. 64 The proposed rule has the potential to threaten public health by creating unprecedented patient and provider confusion by having multiple labels for bioequivalent products. The Committee urges the FDA to finalize the rule based upon comments it received in the docket and during the March 27 public meeting to meet the stated objectives of ensuring that patients have the most complete and up-to-date information regarding their prescription drugs. The final rule should establish: (1) FDA as the final decision maker of whether or not a manufacturer should change its labeling in a multisource environment; (2) a process by which the FDA collects and utilizes all safety information to determine if a labeling change is required—from the new safety information from the manufacturer to sources such as the Sentinel System and other global databases; (3) a process by which the FDA has defined time parameters to take action on new safety information provided by innovator or generic application holders; and, (4) a process by which manufacturers should have a defined time period to make the corresponding labeling change. A final rule with these minimum requirements should be grounded in scientific evidence, and present no opportunity for mismatched dispensing or use information between the innovator drug and the generic version drug.

FDA Response:
The proposed rule is 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.

12. Duchenne Muscular Dystrophy

The Committee is aware that the FDA recently released draft guidance for the development of drugs to treat Duchenne Muscular Dystrophy and related issues. The Committee commends FDA for working with patient groups and urges them to continue this collaborative approach when evaluating the medical needs of a rare disease community.

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 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 guidance and public comment. FDA carefully considered the consortium'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 in 2016. 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, and to serve as a focus for continued discussions on this topic.

13. 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 provides an increase of $2.5 million for the Food Safety Outreach Program under NIFA, and expects that, per the proposal in the President's fiscal year 2016 budget request, 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 existing state and local food programs is critical to achieving high rates of compliance with 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, in addition to contracts, grants, and cooperative agreements and other vehicles for this partnership. Both FDA and NIFA will continue to work with Regional Centers and the National Coordination Center to provide food safety training, education, outreach, and technical assistance at the farm level.

14. 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:
CFSAN will continue to support the Food Contact Notification (FCN) program in FY 2016 with appropriated funding. Over the last three years, more than 100 FCNs per year have become effective. Given the significant number of FCNs received and evaluated per year, however, user fees would improve the program's reliability and predictability. Fees would allow the program to continue to operate at a high level of production, and without disruption, by providing a reliable source of funding. User fees are a particularly appropriate form of support for FCN review because the program provides a specific benefit (authorization to market a food contact substance) to an identifiable entity – the entity submitting the FCN, who is usually the producer of the food contact substance.

15. Generic Drug User Fee Facility Fees

When the FDA begins the process for GDUFA reauthorization negotiations on June 15, 2015, the Committee urges all stakeholders to carefully consider providing fee waivers, exemptions, or otherwise reduced fees for small generic drug manufacturers to minimize the disproportionate financial burden on these companies.

FDA Response:
As part of the GDUFA reauthorization process a small business workgroup was formed between industry and FDA to address this issue and evaluate proposals. At the conclusion of the negotiations, FDA will report out on the proposed GDUFA II agreement.

16. 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 will soon engage in more extensive scientific analysis of the potential risks of genome editing and a broader public discussion of the societal and ethical implications of this technique. 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 actively supports the National Academy of Sciences and National Academy of Medicine study of the scientific, medical, societal, and ethical implications of human germ line gene editing.

FDA acknowledges that the current appropriation directs, "None of the funds made available by this Act may be used to notify a sponsor or otherwise acknowledge receipt of a submission for an exemption for investigational use of a drug or biological product under section 505(i) of the Federal Food, Drug, and Cosmetic Act (21U.S.C. 355(i)) or section 351(a)(3) of the Public Health Service Act (42 U.S.C. 262(a)(3)) in research in which a human embryo is intentionally created or modified to include a heritable genetic modification. Any such submission shall be deemed to have not been received by the Secretary, and the exemption may not go into effect."

17. 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 - in the proposed deeming regulation – 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, in the premarket tobacco application context, the agency's product evaluation 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 also has a regulatory pathway for tobacco products that are sold or distributed to reduce harm or the risk of tobacco-related disease. These products include, for example, 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 Tobacco Control 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. FDA is currently conducting scientific review of eight modified risk tobacco product applications to determine whether the applicant has provided sufficient scientific evidence for FDA to issue a modified risk order allowing the products to be marketed as modified risk.

18. Imported Pet Food Product Transparency

As of May 15, 2015, the FDA had received approximately 5,200 reports of pet illness related to consumption of jerky pet treats, nearly all of which are imported from China. The reports involve more than 6,000 dogs, 26 cats, and 3 humans and include more than 1,100 canine deaths. These incidents date back to 2007. The Committee requests that the FDA provide it with a summary 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 until the issue has been resolved.

FDA Response:
FDA will provide the requested reports.

19. Late Reports

The Committee reminds the Commissioner that the timelines specified by the Committees on Appropriations of the House and Senate for fiscal year 2015 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 has provided the requested reports.

20. Local Port Cooperation

The Committee directs 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:
ORA does extensive work with local ports by working directly with local port authorities and U.S. Customs and Border Protection (CBP) on examination and control of FDA regulated food products at ports. ORA also works with local governments including states on food borne illness outbreaks and capacity in dealing with food borne illness.

21. Mammography Quality Assurance Advisory Committee

More than three 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 to implement the recommended changes and will provide the requested report.

22. 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.

23. Medical Gas Rulemaking

The Committee is concerned that the FDA has not initiated rulemaking to address numerous longstanding regulatory issues for medical gases despite the statutory requirement in FDASIA to issue a final rulemaking addressing all necessary changes for medical gases by July 9, 2016. 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 FDA has never responded to a 1979 Citizens Petition on expiration dating or a 1994 Citizens Petition on calculation of yield, and has not responded to a January 2014 statutorily required report on medical gas regulatory

review. Therefore, the FDA shall issue a proposed rulemaking to address each and every regulatory issue that creates safety and enforcement issues for medical gases by September 30, 2015.

FDA Response:
FDA has taken action on a number of items identified as unaddressed by the Committee. In June 2015, FDA sent the required Report to Congress on our review of Federal drug regulations related to medical gases (the June 2015 Report). FDA also responded to the 1979 and 1994 citizen petitions in June 2015.

As required in FDASIA, FDA reviewed Federal drug regulations that apply to medical gases, and submitted the June 2015 Report to Congress. FDA sought public comments through meetings and a public docket.

As described in that report, FDA has determined that the current regulatory framework is adequate and flexible enough to appropriately regulate medical gases with regard to most issues. FDA can work within the existing regulatory framework to regulate the production and distribution of medical gases without rulemaking through, for example, publication of revised guidance to industry and revisions to FDA's medical gas inspection program and related inspection training. FDA disagrees that these tools are inadequate to appropriately regulate medical gases, and specifically disagrees that the existing regulations have led to any significant safety issues in the provision of medical gases.

FDA is currently engaged in a number of activities intended to reduce regulatory uncertainty and clarify expectations for industry and other stakeholders including additional training of inspectors, implementing an updated inspection program, and updating the 2003 draft guidance for industry on current good manufacturing practices (CGMPs) for medical gases. In December 2015, FDA staff met with representatives of the medical gas industry regarding their views on the revision of the 2003 draft guidance on CGMPs.

As stated in FDA's Report to Congress on the regulation review, FDA has determined that certain regulation changes regarding warning label statements and adverse event reporting are or may be needed, and FDA will continue to evaluate the need for regulatory changes on an ongoing basis. FDA expects to maintain open communication with industry, members of Congress, and other stakeholders as appropriate, and we will continue to evaluate and address medical gas issues as needed.

The statutory deadline set in FDASIA to finalize any regulation changes that FDA has determined are necessary is July 9, 2016 (see FDASIA section 1112(b)). FDA will endeavor to meet that date for any such regulations.

24. Menu Labeling

The Committee is concerned about 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. These newly regulated entities do not have clear guidance from the FDA as to how they must comply with numerous provisions of the final regulation. The Committee includes bill language that directs the FDA to implement the final rule no earlier than December 1, 2016, and at least one-year following agency publication of related guidance to newly regulated stakeholders.

FDA Response:

FDA issued a draft guidance document in September 2015 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 draft guidance responds to the 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.

FDA received substantive and useful feedback in the stakeholder comments on the draft guidance and is working diligently to finalize the guidance. FDA recently extended the date for these covered establishments to comply with the FDA's menu labeling final rule by an additional year, until December 2016, to ensure that companies have adequate time to fully implement the requirements of the rule. During this one-year extension, FDA is continuing to meet with industry and will work flexibly and cooperatively with individual companies making a good faith effort to comply. In addition, we will be providing educational and technical assistance for covered establishments and for our state, local, and tribal regulatory partners to support consistent compliance. FDA believes that this cooperative approach helps to improve the dialogue surrounding the requirements and facilitates successful implementation in a practical way.

25. Off-Label Guidance

The Committee notes that in December of 2011, the FDA issued "Guidance for Industry: Responding to Unsolicited Requests for Off-Label Information About Prescription Drugs and Medical Devices", and a request for comment to assist the agency in evaluating policies for off-label uses of both approved and investigational drugs and devices. The comment period closed on March 27, 2012. Further, the FDA responded in June 2014 to two citizen petitions that were submitted to the agency in July of 2011 and September of 2013 requesting clarification of regulations and policies regarding certain communications related to investigational new drugs and investigational new devices and off-label uses of drugs and devices. In the FDA's response, the agency stated, "that it plans to issue guidance that addresses unsolicited requests, distributing scientific and medical information on unapproved new uses and manufacturer discussions regarding scientific information more generally, by the end of the calendar year." The Committee is concerned that the FDA has yet to issue new guidelines regarding the manner in which truthful and non-misleading scientific information outside of a product label for prescription drugs and medical devices can be conveyed. The Committee directs the FDA to address this issue comprehensively, outlining how manufacturers can communicate with all healthcare stakeholders, and to complete such guidelines within 60 days of enactment of this Act.

FDA Response:
FDA is examining its rules and policies on this issue; the purpose of this review is to help ensure that our implementation of FDA's legal authorities best protects and promotes the public health in view of ongoing developments in science and technology, medicine, health care delivery, and constitutional law. The Agency continues to be actively engaged in this effort and intends to issue new guidance and solicit public input in the near future.

26. Over the Counter (OTC) Medicines for Children

The Committee is concerned that the FDA has not issued a proposed rule revising the monograph regulating the labeling of OTC cough and cold products for children. The

Committee directs the agency to publish a proposed rule by November 30, 2015, based on scientific evidence for safety and efficacy in pediatric populations and taking into consideration the October 19, 2007 joint recommendations of its Pediatric Advisory Committee and Nonprescription Drugs Advisory Committee. While the Committee appreciates the agency's effort to explore possible improvements to the OTC drug monograph process; these efforts should not impede the prompt publication of this proposed rule.

FDA Response:
We share Congress' concerns over the delay in the publication of the Over-the-Counter (OTC) Cold Medicines for Children proposed rule. We have been working diligently on this rule and are committed to its publication.

New scientific methods and considerations for assessing medication use in children, particularly related to cough and cold products, are evolving rapidly and have undergone significant changes since the 2007 joint Pediatric and Nonprescription Drugs Advisory Committee meeting. FDA will continue to identify and assess new scientific methods and considerations for clinical testing of cold and cough medicines in children to develop this rule.

We understand that until this rule is published, consumers may not have the most current information regarding the use of OTC cold medicine products in general and cough-cold products in particular. Therefore, we have published a number of consumer updates (available on the FDA website) to inform consumers on the safe and effective use of OTC cold medicine products.

Examples include a checklist for choosing OTC medicines for children,[109] along with guidance on how to choose medicine for children, [110] using OTC cough cold products in children, [111] and most recently, advice on how to care for infants and young children with a cold.[112]

Finally, FDA held an advisory committee (AC) meeting on December 10, 2015, to review codeine use in children for both analgesic and cough-cold indications. This meeting follows a number of releases by FDA to inform both consumers and health care providers about the safe use of codeine in children. Further information about both the AC meeting and FDA releases about the safe use of codeine can be found online.[113]

While these consumer updates are not a substitution for the proposed rule, they provide consumers with additional knowledge to help ensure the health and safety of their children.

27. Pharmacy Compounding

The Committee is very concerned with the draft MOU that the FDA has proposed under Section 503A of the FDCA. The proposed MOU would complicate patient and prescriber access to compounded medications, and may have a deleterious effect on small pharmacies. Under the draft MOU, the FDA attempts to describe "distribution" as occurring when "a compounded human drug product has left the facility in which the drug was compounded." In the DQSA, Congress only allowed the FDA to regulate "distribution." But the MOU appears to exceed the

[109] Available at: http://www.fda.gov/downloads/drugs/resourcesforyou/consumers/buyingusingmedicinesafely/understandingover-the-countermedicines/ucm094879.pdf
[110] Available at: http://www.fda.gov/drugs/resourcesforyou/consumers/ucm312776.htm
[111] Available at: http://www.fda.gov/downloads/forconsumers/consumerupdates/ucm048524.pdf
[112] Available at: http://www.fda.gov/downloads/forconsumers/consumerupdates/ucm423252.pdf
[113] Available at: http://google2.fda.gov/search?q=codeine&client=FDAgov&site=FDAgov&lr=&proxystylesheet=FDAgov&requiredfields=-archive%3AYes&output=xml_no_dtd&getfields=*

authority granted in the statue by redefining "distribution" in a manner that includes dispensing—something unprecedented. This overreach could generate exactly the kind of costly and confusing litigation that Congress intended to avoid when it amended and reinstated Section 503A. The Committee expects that, when a final MOU is proposed as a model agreement for the states to consider, that distribution and dispensing are treated as the different and separate activities that they actually are.

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).

Congress 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 NABP, FDA is engaging in a public process to obtain comments on the draft standard MOU. FDA is soliciting 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 Intergovernmental Working Meetings 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.

28. 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:
The referenced GAO report addressed both professional and patient labeling. However, the proposed rule pertains only to professional labeling for prescription drugs —it does not propose any changes to the distribution of patient labeling for prescription drugs. Also, the provision on electronic drug labeling may impair FDA's ability to modernize the system for disseminating drug information and take advantage of technological advancements. Such advancements now 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.

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 proposes to require drug manufacturers to provide labeling in paper format to any patient or provider upon request.

29. 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.

30. Scientific Study Data

Sound science, peer review and transparency are essential to effective protection of public health. The Committee is concerned that data from scientific studies utilized in forming public policy may not be available for public review, even under Freedom of Information Act requests. The Committee believes that if public policy is based on a scientific study, that study should be available for public review. The Committee urges the FDA to immediately provide, on its website, the data and studies it uses to support public policy used by the FDA or other Federal agencies based on FDA studies.

FDA Response:

FDA shares the objectives of transparency and maximization of public access to the results of research underlying our regulatory decisions. Accordingly, FDA has issued a Staff Manual Guide 2126.4related to the public access to FDA-funded peer-reviewed publications and digitally stored data. [114] FDA has also established a webpage to inform the public of this new initiative.[115]

With the passage of the Food and Drug Administration Amendments Act of 2007, sponsors of certain clinical trials involving FDA-regulated products also became subject to expanded requirements to publicly disclose information. Furthermore, when FDA approves medical products, FDA regularly publishes on its website non-privileged information regarding the scientific basis for those approvals.

31. Sodium Intake Levels

The Committee is concerned about the FDA's continued focus on voluntary sodium reductions and recommendations to remove the GRAS status of sodium given the growing body of evidence that suggests low sodium consumption can lead to health problems in healthy individuals. The Committee requires the FDA, in coordination with CDC, to convene a panel at the IOM to determine the blood pressure effect and Cardiovascular Disease (CVD) implications for healthy people consuming sodium at 3000 mg or less per day. Federal funds should not be expended on sodium reduction activities below 3000 mg per day until the science is formally considered surrounding healthy and safe sodium intake, especially for healthy individuals, and the impact of lower sodium on blood pressure (and an extrapolation to health), including direct research suggesting a negative impact of lower sodium on health.

FDA Response:
Americans are consuming excess sodium, which contributes to increased risk of hypertension, a primary contributor to stroke and heart disease. FDA and its federal partners, including the CDC, have been focusing on voluntary reductions to move from a current sodium intake of about 3,400 milligrams (mg) in the U.S. to a value closer to 2,300 mg per day.

About 75 percent of sodium in the diet is estimated to be added during the manufacturing of foods and preparation of restaurant foods, making it difficult for consumers to reduce their sodium intake (Anderson et al., 2010; Mattes and Donnelly, 1991). Encouraging industry to reduce sodium in products so consumers have more options does not require bringing consumers into an excessively low sodium intake range. U.S. government efforts are not focused on reducing sodium to below 2,300 mg per day.

The 2013 IOM report entitled *Sodium Intake in Populations: Assessment of Evidence* reaffirmed that sodium intake levels are too high and should be reduced to 2,300 mg per day. This recommendation is also supported by the Scientific Report of the 2015 Dietary Guidelines Advisory Committee (DGAC), which thoroughly considered the 2013 IOM Sodium Report and other evidence in their review, and also the 2015-2020 Dietary Guidelines for Americans.

FDA is aware of recent observational studies (Stolarz-Skrzypek et al., 2011, O'Donnell et al., 2011; O'Donnell et al., 2014; Graudal et al., 2014) that are inconsistent with the large body of evidence that consistently shows a dose-response relationship between sodium intake and blood pressure (Aburto et al., 2013; Sacks et al., 2001; He et al., 2013, Mozaffarian et al., 2014; Eckel et al., 2014).

[114] Available at: http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/StaffManualGuides/UCM479268.pdf
[115] Available at: http://www.fda.gov/ScienceResearch/AboutScienceResearchatFDA/ucm433459.htm

Results of these recent observational studies suggest low- and high-sodium intakes are associated with cardiovascular disease (CVD) events or deaths, and are inconsistent with other observational studies showing lower-sodium intake is associated with lower risk of CVD (Cook et al., 2014; Poggio et al., 2015). Like other studies reviewed by IOM in 2013 and an American Heart Association Scientific Advisory Committee in 2014 (Cobb et al., 2014), these studies have major limitations in the selection of participants and/or measurement of sodium intake. Expert review of these studies by FDA and the Centers for Disease Control and Prevention indicate that these recent observational studies do not shift the weight of evidence.

High blood pressure is a leading risk factor for heart disease and stroke (Stamler et al., 1993; Kannel et al., 1996; van den Hoogen et al., 2000; O'Donnell et al., 1997, Prospective Studies Collaboration, 2002). Reducing average sodium intake in the U.S. population can reduce blood pressure and save tens of thousands of deaths and billions of health care dollars each year (Coxson et al., 2013; Bibbins and Domingo, 2010; Huang et al., 2014a).

32. 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 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:
The FDA Food Safety Modernization Act (FSMA) passed by Congress established requirements for hazard analysis and preventive controls to control hazards in food. FDA is required to implement the preventive controls system for both human and animal food. In its final rulemaking, FDA also established current good manufacturing practice regulations (CGMPs) for animal food.

Some human food processors, including alcoholic beverage production facilities, also produce by-product, such as wet spent grains, for use as animal food. If these processors are already subject to and in compliance with human food CGMPs and applicable human food safety requirements of the FD&C Act and FDA regulations, and they do not further process the by-product, then the preventive controls and CGMP regulations do not apply to the by-product, except limited CGMPs to prevent contamination when holding and distributing the by-product.

FDA is committed to helping ensure that animal food originating from the alcoholic beverage industry is safe for its intended use and not adulterated. Although Section 750 prohibits FDA from using its appropriated resources to implement or enforce any provision of FSMA with respect to the distribution, sale, or receipt of dried spent grain byproducts of the alcoholic beverage production process, FDA can continue to use resources to implement and enforce other applicable provisions of the FD&C Act for these spent grains. For example, any further processing of by-products of the alcoholic beverage industry, such as drying wet spent grains, must be done in accordance with CGMPs.

The CGMP requirements related to further processing human food by-product for use as animal food apply to other types of human food by-product and are not targeted solely to the drying of spent grains. These requirements will be applied consistently across the human food industry to help ensure that when human food by-products are further processed, they are processed in a way that keeps them safe for use as animal food. When processing by-products for use as animal food, a human food facility has the option of following either the human food CGMPs in 21 CFR part 117, subpart B or the animal food CGMPs in 21 CFR part 507, subpart B.

33. Sunscreen Ingredient Applications

The Committee is concerned that another year has passed without the FDA completing its review of the pending Time and Extent Applications (TEAs) and the OTC Monograph rulemakings on sunscreens. Immediate action on sunscreen applications should be a priority since the need for sunscreens is evident by the nearly five million people that are treated annually for all skin cancers and the fact that melanoma is the fifth leading cause of cancer in the U.S. this year. The bill provides the requested funding of $716,000 for the FDA to complete timely reviews of filed requests and determine the safety and efficacy of sunscreen ingredients.

FDA Response:
The Sunscreen Innovation Act (SIA) imposes on FDA strict deadlines for making determinations about the generally recognized safe and effective (GRAS/E) status of these ingredients. It does not relax the scientific standards for evaluating safety and effectiveness or the requirement for sponsors to provide adequate data on which to base a GRAS/E determination.

As per the timelines in the SIA, FDA has completed reviews for all pending Time and Extent Applications for review of nonprescription sunscreen active ingredients and has tentatively determined that the pending sunscreen active ingredients are not GRAS/E for use in OTC sunscreens because the data are insufficient. FDA described the additional data needed to determine that a particular nonprescription sunscreen active ingredient is GRAS/E and not misbranded in the proposed sunscreen orders it has issued under the SIA for each of the pending requests regarding nonprescription sunscreen active ingredients. The data described are in line with the safety data FDA is currently seeking for other topical nonprescription active ingredients under the OTC drug monograph system and for both topical prescription and nonprescription drugs seeking approval under the new drug application (NDA) process.

In addition, FDA has held public meetings with sponsors of pending requests for nonprescription sunscreen active ingredients to discuss data requirements and has issued draft guidance, as required by the SIA, to further delineate safety and effectiveness data needed to make a GRAS/E determination for a nonprescription sunscreen active ingredient. No data have been received, and there are no timelines imposed by the SIA for industry to submit this data. FDA looks forward to receiving and reviewing necessary industry data on which to base a (GRAS/E) determination.

FDA is committed to doing its part to provide American consumers with additional options for safe and effective nonprescription sunscreen active ingredients. However, FDA relies on industry to submit the data needed for review in order to support a GRAS/E determination. Americans deserve sunscreen products that are shown to be safe and effective. FDA has proposed data requirements that will allow us to determine that sunscreen active ingredients are generally recognized as safe and effective for use in nonprescription sunscreens. These data requirements were unanimously supported by a panel of scientific experts at a September 2014 public Advisory Committee meeting on sunscreens.

34. Sunscreen Ingredients and Report

Thirteen years have passed without FDA final decisions on sunscreen ingredients that have been used around the world for many years. FDA's inaction is particularly concerning because bipartisan reforms were enacted in the Sunscreen Innovation Act (SIA) addressing all of the issues identified as impediments by the FDA. The Surgeon General called on the Federal government to work with stakeholders to support skin cancer prevention and yet the FDA has still not approved a new sunscreen product since the 1990s. The FDA shall produce a report to the Committee by September 1, 2015, that contains a detailed analysis of how the FDA is balancing the Surgeon General's Call to Action, 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 posed to human health in FDA's GRAS standard. Furthermore, the FDA shall issue draft guidance for industry outlining data required for sunscreen active ingredients to meet the FDA's safety and efficacy standards and meet SIA's statutory deadlines for publication. The bill provides $716,000 for FDA's sunscreen activities.

FDA Response:
The Sunscreen Innovation Act (SIA) sets forth timelines within which FDA is required to take certain actions on pending and sunscreen Time and Extent Applications (TEAs) and new requests under the SIA. It also imposes on FDA requirements to issue certain guidances, proposed and final rules, and reports to Congress.

The SIA requires FDA to, among other things:

- Issue a notice in the Federal Register of the availability of the feedback letters deemed to be proposed orders under the SIA for the six sunscreen TEAs that had received feedback letters within 45 days of its enactment. – Completed on January 7, 2015.
- Complete evaluation of available data for the two pending sunscreen active ingredient requests that had not received feedback letters at the time of enactment of the SIA and issue proposed sunscreen orders within 90 days – Completed on February 24, 2015.
- Conduct meetings, if requested, with sponsors of each of the eight pending requests that had received proposed sunscreen orders within 45 days of request – FDA has received four requests for meetings and has convened all meetings within the required timeframe
- Issue four draft guidances, including a draft guidance outlining safety and effectiveness data required determining whether a nonprescription sunscreen active ingredients is GRAS/E, within one year of enactment. – Completed on November 20, 2015
- Amend and finalize the sunscreen monograph regulations within five years (November 26, 2019) which will involve issuing a proposed and final rule.

FDA has met its statutory obligations under the SIA to date and appreciates the appropriated funds which will facilitate continuing this important work. FDA now looks forward to receiving and reviewing necessary industry data on which to base a generally recognized safe and effective (GRAS/E) determination for nonprescription sunscreen active ingredients. FDA continues to strive to meet the remaining deadlines, including the report to Congress, and plans to finalize the draft guidance documents in 2016.

35. 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:
FDA continues to be committed to helping sponsors in this area through extensive interactions such as early pre-Investigational New Drug meetings, educational sessions, workshops, advisory committee meeting discussions, and issuance of guidance. Regenerative medicine is a rapidly evolving field that encompasses a broad spectrum of products, such as skin grafts, drugs to help regenerate the liver, artificial organs made of living cells on device scaffolds, and delivery of cells into the brain to restore aspects of function. Regenerative medicine may incorporate use of drugs, biologics, devices, and combinations of these.

Accelerated approval using surrogate or intermediate endpoints is only one regulatory tool that could be utilized in facilitating development and review of regenerative medicine products. Identifying specific surrogate and intermediate endpoints for accelerated approval of regenerative medicine products could be counterproductive, however, because such specifications risk prematurely defining the field in a way that could limit exploration of innovative treatments. Rather, FDA considers proposals for surrogate and intermediate clinical endpoints on a case-by-case basis, in order to allow the greatest regulatory flexibility to facilitate the development of each of these novel products. FDA has an Expedited Programs guidance delineating the use of surrogate and intermediate endpoints for accelerated approval that applies to regenerative medicine products that are drugs and biologics, and a similar guidance for devices.

36. 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 first report shall include a distinct categorization of the user fee balances that are being carried forward into fiscal year 2017 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.