SUMMARY OF FOOD AND DRUG ADMINISTRATION SAFETY AND INNOVATION ACT

TITLE I – FEES RELATED TO DRUGS

Under this section, the drug industry would pay over $700 million in FY 2013 and higher amounts in the remaining four years. In exchange, FDA would commit to the following: (1) meeting performance goals regarding the timely review of drug applications; (2) increasing interaction between drug sponsors and FDA during the review process; (3) improving engagement with patients, including those with rare diseases; (4) providing more granular data from its review divisions to improve transparency, and (5) undertaking an independent assessment by a third party of FDA's performance in FDA's review of applications for novel drugs.

TITLE II – FEES RELATED TO DEVICES

Industry would pay $595 million in user fees for FY 2013-2017 in return for significant changes in FDA performance and accountability. The bill would authorize the following changes: FDA would report its total time for reviewing devices; the review process would include greater interaction between sponsors and the agency; an independent entity would review the device approval and clearance process; and FDA would have to implement a corrective action plan to address deficiencies found in the independent review.

TITLE III: FEES RELATING TO GENERIC DRUGS

This title would authorize the new Generic Drug User Fee Act (GDUFA). The proposed generic drug user fee would provide additional resources for the review and regulation of generic drugs. Under GDUFA, the generic drug industry would pay approximately $1.5 billion over five years. The industry agreed to this fee in return for faster and more predictable review of generic drug applications and increased inspections of drug facilities.

TITLE IV: FEES RELATING TO BIOSIMILAR BIOLOGICAL PRODUCTS

Title IV contains language that would authorize the new Biosimilars User Fee Act (BSUFA). This user fee would apply to products approved under the abbreviated approval pathway for biological products shown to be biosimilar to an FDA-licensed biological product. BSUFA would authorize the following four types of fees: application, product, establishment and biosimilar product development. The first three would be set equal to the PDUFA rate for each type of fee. The product development fee would be set at 10 percent of the PDUFA application fee.

TITLE V: PEDIATRIC DRUGS AND DEVICES

Section 501 would make permanent the Best Pharmaceuticals for Children Act (BPCA) and the Pediatric Research Equity Act (PREA).

Section 502 would clarify the Secretary's authority to award exclusivity for studies conducted pursuant to a written request, including a conforming change for biological products.

Section 503 would require the Secretary to issue guidance providing for Pediatric Review Committee (PeRC) review of any significant modifications made to written requests or pediatric study plans.

Section 504 would require the Secretary, within three years of enactment, to make public the medical, statistical, and clinical pharmacology reviews of written requests made between 2002 and 2007 that resulted in a labeling change.

Section 505 would allow for extensions of pediatric study deadlines in appropriate circumstances. Current tracking requirements would be expanded to collect data about deferral extensions and the timeline to completion of assessments. If a required pediatric study was not completed or deferred, the Secretary would issue a letter and require a response within 45 days, both of which would be made publicly available.

Section 506 would tie the submission of an initial pediatric study plan to the sponsor's end of the phase 2 meeting with FDA, unless the Secretary and the applicant agree to an alternative date. The requirements and process for pediatric study plan submissions would be further clarified through regulations.

Section 507 would reauthorize the Pediatric Advisory Committee, reauthorize the Pediatric Subcommittee of the Oncologic Drug Advisory Committee (ODAC) in a manner consistent with the authorization of ODAC, reauthorize the Humanitarian Device Exemption Extension through 2017, and reauthorize the Program for Pediatric Study of Drugs.

Section 508 would require a report every five years evaluating the effectiveness of BPCA and PREA**.**

Section 509 makes technical changes.

Section 510 would require the Secretary to hold at least one public meeting to discuss ways to encourage and accelerate the development of new therapies for pediatric rare diseases.

Sec. 511 would require FDA's Office of Pediatric Therapeutics to have a neonatologist on staff.

TITLE VI: MEDICAL DEVICE REGULATORY IMPROVEMENTS

Sections 601 would return the Investigational Device Exemption (IDE) approval process to the standard authorized by the statute and implementing regulations. IDEs are needed for manufacturers to conduct clinical trials on devices.

Section 602 would reaffirm the least burdensome provisions added during the Food and Drug Administration Modernization Act of 1997 (FDAMA).

Section 603 would require FDA reviewers to provide a substantive summary of the scientific or regulatory rationale for significant decisions, and it would establish an expedited appellate process for challenging those decisions.

Section 604 would force the withdrawal of FDA's recent guidance documents on medical device modifications and prevent FDA from issuing any new guidance on the subject until it completes a report to Congress on the subject. Until FDA issues a new guidance on the subject, the 1997 guidance would be the standard.

Section 605 would require the Secretary to create a program to assess information submitted or reported pursuant to device recalls, removals and corrections and to use this information to identify strategies for mitigating health risks from defective or unsafe devices. The Secretary would be required to clarify procedures for device recall audit checks and develop criteria for assessing correction or removal actions.

Section 606 would allow the Secretary to issue a clinical hold prohibiting the sponsor of a medical device from conducting a clinical investigation using the device if the Secretary determines the device represents an unreasonable risk to the subjects' safety or for other reasons established by regulation. A sponsor requesting a removal of a clinical hold would be required to receive a written decision within 30 days.

Section 607 would allow the Secretary to classify certain new devices without predicates into class I or II without first issuing a determination that they are not substantially equivalent (NSE) if the devices meets certain risk classification criteria. The Secretary could decline this de novo classification request if the device was not low-moderate risk or if there was in existence a legally marketed device on which to base FDA review.

Section 608 would allow the Secretary, based on new information, to change the classification of a device by administrative order instead of by regulation.

Sections 609-610 would allow FDA to enter into agreements with foreign countries on harmonizing inspections and common international labels of medical devices. It also would provide transparency regarding FDA's involvement in international activities.

Sections 611-612 would reauthorize the third party review and third party inspection programs. This section would reduce costs by allowing to FDA to partner with foreign countries in inspections.

Section 613 would expand the exemption from the prohibition on profit for devices that have been granted Humanitarian Device Exemptions to include devices intended for use in adults if the device is intended for the treatment or diagnosis of a disease or condition that does not occur in pediatric patients, or that occurs in such numbers that the device's development is impossible, highly impracticable, or unsafe. The annual distribution number permitted for HDE devices would be altered to the number of devices needed to treat, diagnose or cure 4,000 individuals in the United States during any calendar year.

Section 614 would require the Secretary to issue proposed regulations establishing a unique device identification system by no later than December 31, 2012, finalize the regulation within six months of the close of the comment period, and implement such a system within 2 years for certain devices, taking into account patient access to medical devices and therapies.

Section 615 would require the Secretary to extend its "Sentinel" postmarket risk identification and evaluation system to include medical devices, and, when implementing this system, to engage stakeholders.

Section 616 would clarify the Secretary's authority to order postmarket surveillance for specified Class II and III devices either at the time of their approval or clearance, or at any time thereafter. A manufacturer would be required to start an ordered postmarket surveillance no later than 15 months after the order.

Section 617 would clarify FDA's policy on customization of devices for small (five or fewer per year), unique populations. If a device is not available in the U.S. and no other devices are domestically available to treat the specific patient, it does not have to comply with the premarket approval requirements for devices if it is intended to meet the special needs of a physician and is manufactured on a case-by-case basis to accommodate the unique physiology.

Section 618 would require the Secretary to issue a report and establish a task force on a proposed regulatory framework pertaining to health information technology software.

Section 619 would clarify that notices that set forth changes in interpretations of a regulation or policy, including notice to industry letters, are guidance documents subject to FDA's good guidance practice rules.

Section 620 would reauthorize, below the current authorization level, demonstration grants for non-profit consortia to promote pediatric device development.

TITLE VII – DRUG SUPPLY CHAIN

Section 701 would expand the information required of registrants engaged in the manufacture, preparation, propagation, compounding, or processing of drugs, to include each facility's unique facility identifier and point-of-contact e-mail address.

Section 702 would require registration by foreign facilities that manufacture, prepare, propagate, compound, or process drugs, by deeming drugs from an unregistered facility misbranded. It would amend registration requirements to include a unique facility identifier and point-of-contact

e-mail address, and to include information about each drug importer and the importer's establishments.

Section 703 would expand the required product listing information to also include information on drug excipient establishments, including a unique facility identifier and point-of-contact e-mail address.

Section 704 would require that, after specifying a unique facility identifier system, the Secretary maintain an electronic database. It also would require the Secretary to ensure the accuracy and coordination of FDA databases in order to identify and inform risk-based inspections.

Section 705 would require the Secretary to carry out drug facility inspections according to a risk-based schedule.

Section 706 would require a manufacturer to submit certain records required for inspection, upon the request of the Secretary, in a timely and reasonable manner at the manufacturer's expense. It also would require the Secretary to clearly describe records requested and to provide a confirmation receipt.

Section 707 would bar the entry of imported drugs from an establishment that is deemed to have delayed, limited or denied an inspection.

Section 708 would allow FDA to destroy counterfeit or adulterated imported drug products after adequate notice.

Section 709 would allow FDA to detain, for a reasonable period, drugs found during inspection which the inspecting officer has reason to believe are adulterated or misbranded.

Section 710 would allow the FDA to share certain information with trusted foreign countries to better leverage resources.

Section 711, with respect to criteria for determining a drug to be adulterated, would clarify that "current good manufacturing practices" include quality controls in manufacturing and assurance of raw material safety.

Section 712 would allow FDA to take into account the inspections of trusted foreign government when considering the risk of an establishment.

Section 713 would allow the Secretary to require electronic submission of certain information by a drug importer as a condition of granting entry. Such information could include regulatory status, facility information (including unique facility identifier), and inspection and compliance information. The Secretary must take into consideration the type of import, such as whether the drug is for import into the United States for use in preclinical or clinical investigation.

Section 714 would require drug importers to register with the FDA.

Section 715 would require those engaged in the manufacture, preparation, propagation, or processing of a drug to notify FDA if it knows the use of the drug could lead to serious injury or death, if the drug is stolen, or if it is counterfeited.

Section 716 would enhance the penalty to not more than 20 years imprisonment or a fine of not more than $1 million, or both, for any person who knowingly and intentionally adulterates a drug under certain statutory definitions of adulteration if the drug has a reasonable probability of causing serious adverse health consequences or death.

Section 717 would enhance the penalty to not more than 20 years imprisonment or a fine of not more than $4 million, or both, for persons who knowingly and intentionally commit certain prohibited acts related to forging and counterfeiting of drugs, including selling and dispensing. It would also amend the federal criminal code to establish criminal penalties of a fine, imprisonment for not more than 20 years, or both for trafficking, or attempting to traffic, in counterfeit drugs. Directs the United States Sentencing Commission to review and, if appropriate, amend its guidelines and policy statements applicable to persons convicted of this offense to reflect congressional intent that such penalties be increased.

Section 718 would provide for explicit extraterritorial federal jurisdiction over a violation of the Federal Food, Drug and Cosmetic Act so U.S. authorities could hold accountable those violating the Act, like those who caused the heparin deaths.

TITLE VIII: GENERATING ANTIBIOTIC INCENTIVES NOW

Section 801 would provide incentives for development of new qualified infectious disease products (QIDPs) by providing an additional five years of market exclusivity, in addition to the periods of exclusivity for which such drugs would otherwise qualify. Sec. 801 defines QIDPs as antibacterial or antifungal drugs intended to treat serious or life-threatening infections. The Secretary would be required to develop a list of pathogens that cause serious or life threaning infections.

Section 802 would make QIDPs eligible for priority review and **Section 803** would make them eligible for fast track review.

Section 804 would require the Secretary to review and, if needed, to update guidance documents regarding the conduct of clinical trials for antibacterial and antifungal drugs, and would allow the Secretary to provide written recommendations for such trials, upon the request of a sponsor seeking approval of a QIDP.

Section 805 would require a reassessment of the antibiotic incentives within 5 years.

Section 806 would require FDA to issue a guidance focused on pathogen-focused antibacterial drug development.

TITLE IX—DRUG APPROVAL AND PATIENT ACCESS

Section 901 contains a sense of Congress that FDA should help expedite the availability of such drugs while maintaining safety and effectiveness standards. This section would require the Secretary to facilitate the development and expedite the review of a drug designated a "fast-track product" (i.e., a drug that is intended for the treatment of a serious or life-threatening disease or condition, and that demonstrates the potential to address unmet medical needs for such a disease or condition) and it enhances "accelerated approval" provisions in the FFDCA (for drugs for serious or life-threatening diseases or conditions including, but not limited to, fast-track products) by clarifying the types of evidence and endpoints on which the Secretary can rely.

Section 902 would require the Secretary to expedite the development and review of a drug designated a "breakthrough therapy." To achieve this designation, a drug must be intended to treat a serious or life-threatening disease or condition, and preliminary clinical evidence must indicate that it may demonstrate substantial improvement over existing therapies.

Section 903 would require the Secretary to ensure that opportunities exist for consultation with stakeholders from the rare disease community and to maintain a list of external scientific and medical experts to consult on products for rare diseases.

Section 904 would require the development of best practices on access to information on prescription drug labels for individuals who are blind or visually impaired, and a GAO to study utilization of such best practices.

Section 905 directs the Secretary to use a consistent and systematic approach to incorporate risk-benefit into regulatory decision making and to communicate the benefits and risks of new drugs.

Section 906 would reauthorize the Orphan Products Grant Program through 2017 and clarify which products are eligible for program grants.

Section 907 would require the Secretary to publish on the Internet website of the FDA a report examining the extent to which current requirement for clinical trial participation and the inclusion of safety and effectiveness data by demographic subgroups including sex, age, race, and ethnicity, are included in applications submitted to the FDA, and to provide such report to Congress.

Section 908 would create a demonstration project that provides priority review vouchers to companies that develop a drug for a pediatric rare disease. The voucher would be redeemed by the company for a subsequent application or could be transferred to another company. The section would require the GAO to conduct a study for Congress on the effectiveness of the program within one year after the issuance of the third priority review voucher. The Secretary could no longer issue new priority review vouchers one year after the third voucher is issued so Congress may determine whether to continue the incentive.

TITLE X: DRUG SHORTAGES

Section 1001 would modify existing reporting requirements for manufacturers of drugs that are life-supporting, life-sustaining, and intended for use in the prevention or treatment of a debilitating disease or condition, including those used in emergency medical care or surgery. The section would authorize the Secretary to expedite establishment inspections and review of supplements and applications that could help mitigate or prevent a "shortage," as defined in this title. It would authorize the Secretary to apply this section, by regulation, to biological products, although the Secretary must consider if the notification requirement for vaccines could be met through the CDC vaccine shortage notification program.

Section 1002 would require the Secretary to establish a task force to enhance the Secretary's response to shortages, and create a strategic plan to address stated aspects of shortages.

Section 1003 would require FDA to maintain a drug shortage list and provide patients, providers and the public with such information in order to prevent, mitigate, and manage drug shortages on the ground. The bill includes safeguards that would prevent the release of confidential business information or information that could adversely affect public health.

Section 1004 would require the Drug Enforcement Administration (DEA) to provide timely approvals or denials of increases in quotas of controlled substances in instances where such an increase could help address a drug shortage.

Section 1005 would require DEA to report annually on their efforts on drugs shortages based on the metrics set forth by Congress.

Section 1006 would allow hospitals within the same health system to repackage drugs into smaller units to alleviate drug shortages.

Section 1007 would authorize GAO to conduct a study to examine the causes of drug shortages and issue recommendations on how to prevent or alleviate a drug shortage. This provision would provide needed data on how the regulatory framework, manufacturing challenges, or other factors contribute to drug shortages, as well as recommendations to address such issues.

TITLE XI—OTHER PROVISIONS

Section 1101 would reauthorize, through October 1, 2017, a sponsor's ability to receive separate approval and exclusivity for a drug containing a single enantiomer, when the racemic drug has already been approved.

Section 1102 would reauthorize, at the current authorization level, the Critical Path Public-Private Partnerships to foster medical product innovation through FY 2017.

Sections 1111 through 1113 would streamline and modernize the regulation of medical gas.

Section 1121 would require the Secretary to issue a guidance document that describes FDA policy regarding the promotion of FDA-regulated medical products using the Internet (including social media).

Section 1122 would task the Secretary of HHS with reviewing and reporting on current Federal initiatives and identifying gaps and opportunities with respect to ensuring the safe use of prescription drugs with the potential for abuse. The Secretary also must issue a guidance document on the development of abuse-deterrent drug products.

Section 1123 would require FDA to work with other peer regulators to reduce duplication of studies necessary for premarket approval, without altering the current standards for premarket review of medical products. It would require FDA, when considering drug and device applications, to either accept foreign clinical data or notify the sponsor of FDA's rationale for concluding that the data are not adequate to support approval, licensure or clearance under applicable FDA standards.

Section 1124 would require FDA to establish a strategy and implementation plan for advancing regulatory science. The report will include priorities related to medical product decision-making and regulatory and scientific gaps. FDA will report annually for FY 2013-2017 on these goals.

Section 1125 would require FDA to report on a comprehensive information technology strategy plan consistent with GAO recommendations, and GAO will report on the progress of FDA to meet the goals set out in such plan.

Section 1126 would require the Secretary of HHS to continue its current activities related to enhancing the scientific knowledge of nanomaterials.

Section 1127 would require the GAO to examine problems posed by online pharmacy websites that violate state or federal law.

Section 1128 would require FDA to submit a report to Congress regarding issues related to small businesses, including opportunities and resources that FDA makes available to small businesses.

Section 1129 would extend whistleblower protections to the Commissioned Corps of the Public Health Service Act.

Section 1130 would codify the compliance date of FDA's regulation, "Labeling and Effectiveness Testing; Sunscreen Drug Products for Over-the-Counter Human Use''.

Section 1131 would require the Secretary to submit an integrated management strategy to Congress. The plan must identify goals and priorities for CDER, CBER and CDRH and describe the actions FDA will take to develop the workforce at these centers.

Section 1132 would make the Risk Evaluation and Mitigation Strategy (REMS) system more efficient by allowing for minor modifications of a drug's REMS. Certain drugs are required to have REMS to ensure that the benefit of the drug outweighs the risk. Currently the law is

unclear as to whether sponsors can make minor modifications to the REMS without the need to have a full reassessment of the REMS.

Section 1133 would extend the timeline for generic forfeitures. Under current law, if a generic drug manufacturer challenges a brand manufacturer's patent as being either invalid or would not be infringed, and if it is the first generic drug manufacturer to make such challenge or makes it on the same day as the first challenger, it can be awarded 180 days of exclusivity from other generic competition. Except in certain circumstances, if FDA does not grant tentative approval within 30 months of the filing of the generic drug application, the generic company forfeits the 180-day exclusivity period. The provision would temporarily increase that tentative approval time period to 40 months. (The current average time for FDA to approve a generic drug application is 32 months.) This 40-month period would be gradually phased back down to 30 months as the FDA eliminates the backlog of pending generic applications pursuant to the generic drug user fee agreement.

Section 1134 would set a date certain for the review of the review of reference listed drug petitions. Current law allows FDA to deny a generic application if the drug the generic application is referencing was withdrawn for safety or effectiveness reasons. Current FDA regulations allow a company to petition the FDA to determine if the reference drug was withdrawn for safety or effectiveness reasons. However, there is no timeframe under which the FDA must respond to the petition, and there have been instances of decision times lasting over two years. This section would require the FDA to respond to these petitions within 270 days which should result in the quicker approval of generic drugs.

Section 1135 would set new rules regarding the review of certain citizen petitions regarding generic and biosimilar applications. Certain citizen petitions ask the agency for a stay of action related to FDA approval of a pending application submitted under section 505(b)(2) (a new drug application that relies on safety and efficacy data produced by someone else) or 505(j) (generic application) of the Act due to scientific or medical questions about the application. The FDA is required to take final agency action on the petition within 180 days. This section would require the FDA to take final agency action on the petition within 150 days. This section also would apply to biosimilar applications which are applications filed under 351(k) of the Public Health Service Act.

Section 1136 would require electronic submission of drug, generic drug, biologic, and biosimilar applications following issuance of a final guidance by the Secretary.

Section 1137 would require the Secretary to develop and implement strategies to solicit the views and perspectives of patients during the medical product development process and regulatory discussions.

Section 1138 would require FDA to develop a communication plan to inform and educate health care providers and patients, on the benefits and risks of medical products, with a particular focus on underrepresented subpopulations, including racial subgroups.

Section 1139 would require FDA to hold a public meeting on the scheduling of hydrocodone.

Section 1140 would require GAO to conduct a study on electronic drug labeling.

Section 1141 would allow the Secretary of HHS to facilitate the exchange of prescription drug information across state lines to prevent abuse and would require a report on such facilitation.

Section 1142 would improve FDA's conflict of interest rules so the agency's advisory committees have access to the most knowledgeable experts. Congress established these rules as part of the 2007 reauthorization, and they have led to significant vacancy rates, especially for advisory committees for rare diseases.

Section 1143 would prohibit the FDA from issuing guidance on the regulation of laboratory developed tests unless it notifies the Committee of its intent to take such action 60 days prior to the issuance of the guidance. This prohibition would end in five years.

Sections 1151 through **1153** would amend the Controlled Substances Act and designate certain synthetic substances as schedule I drugs.