Summary of the Drug Safety Enhancement Act of 2011, H.R. 1483

Filed on: **April 12, 2011**

Sponsors: **Rep. Dingell (D-MI), Rep. Waxman (D-CA), Rep. Pallone (D-NJ) and Rep. DeGette (D-CO)**

Initial Status: Referred to the House Committee on Energy and Commerce

TITLE I – PREVENTION

Sec. 101 – Registration of producers of drugs; applicable fee

- Drugs manufactured, prepared, propagated, compounded, or processed at unregistered sites are deemed misbranded. The Secretary of Health and Human Services (HHS) may suspend registration for violation of the Federal Food Drug, and Cosmetic Act (FDCA), or for knowingly or repeatedly making an inaccurate or incomplete statement or submission relating to the manufacture, preparation, propagation, compounding, processing, or importing of a drug. The Secretary may also cancel registration if false or incomplete information is provided or if the registration fee has not been paid.
- Excipient manufacturers will also be required to register under section 510 of the FDCA 18 months after enactment. The Secretary is required to update the regulations for registration within six months of enactment.
- Entities that list drugs as part of registration under section 510 of the FDCA must also list all active and other ingredients for each drug listed.
- Registration fees will be collected to defray the increased costs of drug safety activities.
    - Costs include: officers, employees, contractors, and advisory committees; lab space; IT; facility leases, maintenance and repair; fee collection.
    - Activities include: those related to compliance with the FDCA, such as standards development, risk assessments and risk communication, inspection planning and inspections, third party inspections, compliance review and enforcement, information technology support, test development, product sampling, administrative detention.
- Registration fees are due 90 days after enactment or December 31, 2011, whichever comes first; December 31 for subsequent years.
- Annually, fee levels will adjust with inflation. Fees will be refunded unless FDA salaries and expenses also increase at least at the rate of inflation.

- The Secretary has the discretion to waive or reduce fees if necessary to protect public health or if the fee would cause economic hardship. Unpaid fees will be treated as a claim of the U.S. Government. The Secretary shall report to congress annually on fee implementation and use. Fees sunset in Fiscal Year 2016 based on the FDCA authorization period for fee collection.

Sec. 102 – Drug supply quality and safety

- "Drug components" include Active Pharmaceutical Ingredients (APIs) or bulk drug substances; inactive ingredients; intermediates of active ingredients whether or not they appear in the finished product; and any original source material regardless of if it appears in the finished product or if it is derived from chemicals, humans, animals, plants, or other materials.
- "Effective Quality Systems" need to be in place two years after enactment. A drug is considered adulterated if the manufacturer is in violation of these requirements. Effective Quality Systems include all of the following components:
    - Management responsibility. The manufacturer shall ensure: adequate resources provided for current good manufacturing practice (cGMP) compliance; procedures established to ensure timely communication of quality issues to management; periodic reviews of process performance and product quality; executive management evaluation of these periodic reviews to determine any appropriate action; integrity and accuracy of data, records, and submissions.
    - Quality responsibility. The manufacturer shall establish and maintain an internal, independent unit to ensure cGMP compliance, and establish procedures to ensure discrepancies are identified and fixed, and ongoing data review to identify trends that might affect product quality and timely actions to prevent any adverse effect on product safety, identity, quality, strength, or purity.
    - Risk management. The manufacturer shall establish and maintain risk management procedures to identify, monitor, and evaluate all factors that can reasonably affect safety, identity, quality, strength, purity or security.
    - Supply Chain Management. The manufacturer shall establish and maintain procedures to ensure safety, identity, quality, strength, purity, and security of all drugs and other materials. The manufacturer shall not continue to receive any source materials or drugs from any person who fails to implement timely correction for supply chain management practices. Supply Chain procedures shall address the entire supply chain from original source materials to the manufacturer, and shall include:
        - acceptance and rejection criteria and a sufficient impurity profile for each component (licensed biological products excluded);
        - on-site audits by a qualified individual before supply begins and at appropriate frequency;

        - requirements for quality agreements with suppliers that address all applicable cGMPs;
        - information sharing from supplier to manufacturer on changes, discrepancies, defects in materials or operations;
        - provision of a certificate of analysis by the supplier for each batch and lot, including complete source, manufacturing, test information and results;
        - methods adequate to detect or exclude the possibility of any substance that may reasonably be expected to indicate a risk to safety, identity, quality, strength, purity or security and to detect or exclude possibility of other risks to safety, identity, quality, strength, purity or security.
    - Manufacturers must evaluate and, where necessary, revise methods based on risk; must evaluate every drug batch and lot made under any revised methods; and must notify the Secretary of any method revision and rationale. The Secretary may require a manufacturer to revise or adopt methods.
    - Manufacturers shall maintain records to document compliance with quality system requirements for two years after expiration date of each drug. Records shall be provided to the Secretary upon request and are also subject to copying during inspection.
    - The Secretary may add further provisions to the quality system requirements. Manufacturers may petition for exemption from any requirement. If the Secretary grants an exemption or variance to more than one manufacturer, the Secretary shall publish a notice thereof in the Federal Register.
- Documentation of supply chain: Manufacturers must provide to the Secretary, upon request, information on where drug and raw materials were produced including preceding producers, manufacturers, distributors and shippers, and information establishing that the drug and ingredients were produced under conditions ensuring identity, strength, quality, and purity.

Sec. 103 – Inspection of producers of drugs

- Every finished dose drug and API manufacturer shall be inspected at least once every two years beginning with the date of registration, or once every four years if the Secretary determines sufficient information exists to assess risk and inspect less often.
- The Secretary shall inspect the drug establishment before the drug enters the U.S. market if the finished dose or API is new or if the drug has undergone a major change requiring prior approval. However, the Secretary may opt not to perform such an inspection if the Secretary determines it is unnecessary based on inspection history.
- The Secretary shall establish information systems capacity sufficient to assess risk and shall develop a risk-based cGMP surveillance and inspection schedule, which shall be implemented within three years of enactment. The risk-based system shall include

product class and associated risks, the date of last inspection, compliance and safety history, shipping volume and history, and other factors as determined by the Secretary.

- The Secretary may inspect excipient establishments to the same extent as any other drug establishment.
- The Secretary shall submit annual reports to Congress on the funding dedicated to inspections of drug establishments and the number of establishments with modified inspection frequencies based on the new risk-based schedule.
- The GAO shall submit a report to Congress on the risk-based cGMP surveillance and inspection system within three years of enactment.

Sec. 104 – Prohibition against delaying, limiting, or refusing inspection

- A drug shall be deemed adulterated if it has been manufactured, processed, packed or held in any establishment, factory or warehouse that has delayed or limited an inspection or refused entry.

Sec. 105 – Clarification of inspection authority related to BIMO and IRB inspections

- Permits inspections of clinical investigation premises.

Sec. 106 – Notification, non-distribution, and recall of adulterated or misbranded drug products

- Failure to notify the Secretary of an adulterated, misbranded, or otherwise harmful product in distribution and failure to comply with an order to recall are prohibited acts.
- A person required to register under the FDCA who believes a distributed drug is adulterated, misbranded, or may cause illness or injury must notify the Secretary of the drug's location and identity as soon as possible.
- The Secretary may request that any person who distributes a drug that the Secretary believes to be adulterated, misbranded, or otherwise in violation of this act to conduct a voluntary recall and notify affected individuals.
- The Secretary may require any person distributing a drug to cease distribution if the Secretary has reason to believe that use of or exposure to the drug may result in illness or injury. The person may appeal, and an informal hearing shall be held within five days of the appeal. The Secretary shall determine whether the order should be amended to require recall.
- After allowing for an informal hearing, the Secretary may order a recall. The amended recall order shall include a specific timetable, require progress reports to the Secretary, and provide for notice to affected individuals.
- If the Secretary has credible evidence that a drug presents an imminent threat of serious adverse health consequences or death, the Secretary may order an immediate "emergency recall" and provision of notice to affected individuals. Persons subject to an emergency recall may appeal within 24 hours but shall conduct the recall notwithstanding the

pending appeal. The appeal must occur within five days and the order may be vacated if the Secretary determines there are inadequate grounds to support the recall order.

- The Secretary may provide notice of a recall to consumers and state and local health officials.
- Drugs subject to a recall or cease distribution order shall be refused admission at the border.
- Notification requirements and the Secretary's recall authorities shall take effect within one year of the enactment date, as determined by the Secretary.

Sec. 107 – Notification

- The Secretary may require wholesale drug distributors, persons required to register, or any other person that distributes drugs except for retail sale to notify the Secretary of:
    - use of or exposure to a drug which may result in illness or injury to humans or animals;
    - significant loss or theft of a drug;
    - Reasonable probability that a drug has been or is being counterfeited;
    - repeated failures by a component manufacturer to ensure compliance with quality systems;
    - any incident causing a drug to be mistaken for, or its labeling applied to, another drug;
    - any contamination or significant chemical or physical change or deterioration after distribution, or any failure of a distributed lot to meet an established specification; or
    - any other information the Secretary deems necessary for the protection of public health.
- The Secretary shall establish the manner of notification through regulation.
- Information exchange provisions allow the Secretary to share trade secret information privately (if the Secretary receives adequate assurances that the recipient will preserve confidentiality) with other federal agencies acting within the scope of its jurisdiction, state and local governments, any person the Secretary determines appropriate, and foreign government agencies or international organizations in order to facilitate global standards harmonization or to coordinate public health efforts. The Secretary may also disclose trade secret information to the public if necessary to protect the public health.
- The Secretary shall not disclose trade secret information received when such disclosure is precluded as a condition of the provider providing the information, unless under court or Congressional order to disclose.

TITLE II – RESPONSE

Sec. 201 – Administrative detention

- The FDA may order detention of a drug believed to be in violation of the FDCA. The detention period is not to exceed 20 days, except where the Secretary determines more time is needed to institute an action, then not to exceed 60 days. Detention orders must be approved by an officer designated by the Secretary.
- Detention orders may require special labeling or marking of detained drugs, and may require that the drug is taken to a secure facility. Detention orders may be appealed, in which case an informal hearing must be held within 15 days of the appeal. Detained drugs shall not be moved from the detention location until ordered by the Secretary or the detention time period expires (with minor exceptions).
- This section shall apply 180 days after enactment. The Secretary shall issue regulations to implement administrative detention provision. Movement of a detained drug or removal of special labeling are prohibited.

Sec. 202 – Destruction of adulterated, misbranded, or counterfeit drugs offered for import

- The Secretary of the Treasury shall destroy any drug that the Secretary of HHS determines to pose a reasonable probability of causing a significant adverse health effects or a drug that is valued at $2,000 or less. (Dollar threshold may be increased by the Secretary of the Treasury.)
- The opportunity for an informal hearing shall be offered after destruction has occurred for drugs that pose health risks or are valued under $2,000, and before destruction has occurred for other drugs. The Secretary of HHS will establish regulations regarding notice and hearing process.
- This section shall go into effect 90 days after the date of enactment.

Sec. 203 – Criminal penalties

- Criminal penalties of up to 10 years in prison and/or fines in accordance with Title 18 of the United States Code for the knowing violations of the FDCA's sections on: adulteration, misbranding, delivery or receipt of adulterated or misbranded product, refusal of inspection, counterfeiting, adulteration of labeling, or providing false clinical trial information.[1]

Sec. 204 – Civil penalties

- Civil penalties are set at $500,000 per violation per day for violations of the FDCA related to drugs. Cap of $10 million for all violations adjudicated in a single proceeding.

[1] Penalties for knowing violations of the FDCA are currently 3 years in prison and/or a $10,000 fine for most violations.

Sec. 205 – Seizure

- For drugs subject to seizure, the seizure process is not governed by Rule G of the Supplemental Rules of Admiralty or Maritime Claims and Asset Forfeiture Actions. For all seizures of drugs brought under this section, exigent circumstances shall be deemed to exist, and a summons and arrest warrant shall be issued by the clerk of the court without court review.

Sec. 206 – Asset forfeiture

- Criminal forfeiture: any person convicted of a violation of FDCA prohibited acts (regarding drugs) shall forfeit to the U.S. any property traceable to the gross proceeds obtained as a result of the violation.
- Civil forfeiture: property traceable to gross proceeds obtained as a result of a violation is also subject to civil forfeiture.

TITLE III – IMPORTATION AND EXPORTATION

Sec. 301 – Documentation for admissibility of imports

- The Secretary may require documentation for imported drugs. The Secretary may develop regulations and where relevant shall consult with Customs and Border Protection. Drugs without required documentation shall be refused admission, and submission of inaccurate or incomplete information required at import or failure to submit such information is prohibited.

Sec. 302 – Registration for commercial importers; fee

- Registration
    - Importers of drugs must register with the Secretary and submit unique identifiers. Maintenance of registration is contingent upon adherence to Good Importer Practices (GIP) to be promulgated by the Secretary in consultation with Customs and Border Protection. Differences in importers and types of imports may be taken into consideration.
    - GIP shall ensure that importers: have adequate information about the imported article, its hazards, and the applicable requirements of the FDCA and the Public Health Service Act (PHSA); have information or procedures adequate to verify that the article and person that produced, manufactured, processed, packed, transported, or held the article are in compliance with the FDCA and PHSA; and have adequate procedures to take corrective action such as the ability to trace, withhold and recall articles if the importer is not in compliance with the FDCA or PHSA.
    - The Secretary may suspend registration for violation of the FDCA or for knowingly or repeatedly making inaccurate or incomplete statements or submissions of information. The Secretary may cancel registration if it contains

false, incomplete, or inaccurate information, is not updated as required, or if the registration fee has not been paid.
    - Failure to register is prohibited; drugs offered for import by an unregistered importer are deemed misbranded.
    - The Secretary shall establish an exemption for importations for personal use and may establish other exemptions.
    - The Secretary shall promulgate regulations to carry out this section within 36 months of enactment. The Secretary shall provide for a reasonable period of time for importers to achieve compliance when setting an effective date for the regulations, taking into account differences among importers, imported products, and related risk.
    - This section takes effect 24 months after enactment.
- Registration fee
    - The importer registration fee shall be $500 for FY 2012, adjusted for inflation in subsequent years.
    - The importer fee is waived if the importer is also subject to a manufacturing establishment registration fee.
    - Importer fees shall only be used to cover costs associated with registering importers and ensuring compliance with good importer practices.
    - Importers shall submit to inspections of their facilities, and permit inspectors to access, copy and verify related records.

Sec. 303 – Registration for customs brokers

- Customs brokers of drugs must register with the Secretary in a manner to be specified by the Secretary and must submit unique identifiers.
- Failure to register is prohibited; drugs offered for import by an unregistered customs broker are deemed misbranded.
- The Secretary may cancel registration if false or incomplete.
- The Secretary shall establish an exemption for importations for personal use, and may establish other exemptions.
- Customs brokers are not subject to civil penalties for failure to submit import documentation.
- The Secretary shall establish regulations within 24 months of enactment. This section shall take effect 24 months after enactment.
- Customs brokers shall submit to inspections of their facilities, and permit inspectors to access, copy and verify related records.

Sec. 304 – Exportation certificate program

- Persons exporting U.S. approved drugs from another country may request an export certificate. The Secretary shall provide such a certificate within 20 days if the request

demonstrates the drug meets applicable requirements of the FDCA. Secretary may determine the form and basis of the certification.

- The Secretary may charge a fee for export certification, not to exceed the amount reasonably related to the cost of issuing such certificates.

Sec. 305 – Extraterritorial jurisdiction

- There is extraterritorial jurisdiction over any drug-related violation of the FDCA if the drug was intended for import into the U.S. or if any act in furtherance of the violation was committed in the U.S.
- Production, manufacturing, processing, preparation, packing, holding or distribution of an adulterated or misbranded drug with the knowledge or intent that such drug will be imported into the U.S. is prohibited.

Sec. 306 – Dedicated foreign inspectorate

- The Secretary shall establish and maintain a dedicated foreign inspectorate, staffed and funded to conduct foreign inspections at a frequency at least equivalent to the domestic inspection rate.

TITLE IV – MISCELLANEOUS

Sec. 401 – Unique identification number for establishments, importers, and custom brokers

- Persons required to register under section 510 (manufacturing sites) shall submit a unique identifier at the time of registration.
- Persons required to register under sections 801(t) or (u) (importers and customs brokers) shall submit a unique identifier for the principal place of business at the time of registration.
- The Secretary may specify by guidance the unique numerical identifier system, and the form, manner, and timing of submissions. The Secretary shall take into account existing systems and compatibility with Customs' automated systems.
- Drugs offered for import will be refused unless appropriate identifiers are provided.

Sec. 402 – Country of origin labeling

- Within three years of enactment, the Secretary shall promulgate regulations to require manufacturers' company websites to list the country of origin of each active ingredient and the place of manufacture for the finished dose drug. Without such information, the finished dug is deemed misbranded. The requirements take place four years after the date of enactment.

Sec. 403 – False or misleading reporting to FDA

- The submission of a false or misleading report required under FDCA related to drugs is prohibited.

Sec. 404 – Subpoena authority

- The Commissioner may issue subpoenas of witnesses, records and other things for drug-related violations of the FDCA, PHSA, and the Federal Anti-Tampering Act.
- The U.S. District Court for the District of Columbia shall have jurisdiction to take action regarding compliance with a subpoena order for persons not within the territorial jurisdiction of the U.S.
- Refusal to obey a subpoena is a prohibited act. A drug may be refused admission at the border if a person who manufactures, processes, packs, holds or ships the drug refuses to obey a subpoena related to that product.

Sec. 405 – Whistleblower protections

- Whistleblower protections cover officers, employees, contractors, subcontractors or agents of people who submit or are required to submit information under the FDCA or the PHSA with relation to drugs.

Sec. 406 – Rule of construction

- Nothing in this legislation affects any authority or requirement related to devices.