McDermott Will & Emery

President Obama Signs Bipartisan FDA User Fee Legislation

July 11, 2012

On July 9, 2012, President Obama signed legislation that reauthorizes the U.S. Food and Drug Administration (FDA) to assess user fees to support the agency's review of marketing applications for drugs (including biologics) and medical devices, and, for the first time, authorizes the FDA to collect user fees on applications for generic drugs and biosimilars. The legislation, which is known as the Food and Drug Administration Safety and Innovation Act, also includes several provisions related to the FDA's review and oversight of drugs, medical devices and biologics.

As expected, the law is a hybrid of the user fee bills approved in the Senate and House, respectively.[1] The following table provides a brief overview of the manner in which the bill originally approved by the Senate, the bill originally approved by the House and the enacted law address various issues related to the regulation of drugs, medical devices and biologics.

Issue	Original Senate-Approved Bill (S. 3187)	Original House-Approved Bill (H.R. 5651)	Final Enacted Law
Medical Devices			
Device reclassification procedures	Would allow the FDA to change a device's classification by administrative order (as opposed to by regulation, as is currently required) New procedure would require publication of a proposed reclassification order in the Federal Register, a meeting of a device classification panel, and consideration of comments to a public docket prior to issuance of a final reclassification order	No comparable provision	Comparable to Senate provision, except: • Adds requirement that the proposed reclassification order set forth the proposed reclassification and a substantive summary of the valid scientific evidence concerning the proposed reclassification
Conditioning premarket approval of a medical device on performance of post-market studies	Would allow the FDA to require, as a condition of its approval of a premarket approval application (PMA), that the applicant conduct a post-market study regarding the newly approved device	No comparable provision	Provision not included in final bill
Post-market surveillance	Clarifies that the FDA may order post-market surveillance of a Class II or Class III device "at the time of approval or clearance of a device or any time thereafter" Would also require the	No comparable provision	Comparable to Senate provision

[1] For more information, see McDermott's *On the Subject* "Senate Easily Passes FDA User Fee Bill, Reconciliation with House Version Looms," and McDermott's *White Paper* "House Passes FDA User Fee Bill; Congress on Track to Pass Reconciled Bill by Beginning of July."

Issue	Original Senate-Approved Bill (S. 3187)	Original House-Approved Bill (H.R. 5651)	Final Enacted Law
	manufacturer to commence the surveillance within 15 months of the issuance of the order		
Sentinel (FDA's post-market risk identification and analysis system)	Would require the FDA to extend Sentinel to include medical devices (requirement only currently applicable to drugs)	Comparable to Senate provision	Comparable to Senate and House provisions
Implementation of a unique device identifier system for medical devices	Would require the FDA to issue proposed regulations establishing a unique device identification system by December 31, 2012 Would also require the FDA to finalize the regulations within six months of the close of the comment period on the proposed rule	Would require the FDA to promulgate regulations implementing a unique device identification system within 120 days of the bill's enactment	Comparable to Senate provision
Agency documentation of medical rationale for decisions relating to medical device marketing applications	Would require the FDA to provide a "substantive summary of the scientific and regulatory rationale" for its decisions to deny a premarket clearance submission under section 510(k), PMA or an investigation device exemption application (IDE) Would give applicants an opportunity to request "supervisory review" of adverse decision	Would require the FDA to completely document the scientific and regulatory rationale for "any significant decision" relating to a 510(k), PMA or IDE; the documentation must reference "significant controversies or differences of opinion, and the resolution of such controversies or differences of opinion" Would also give applicants an opportunity to request "supervisory review" of a "significant decision"	Comparable to House provision, except: • Requires "substantive summary" (as in Senate version) of scientific and regulatory rationale instead of requiring the agency to "completely document" its decision
De novo medical device classification	Would allow the FDA to classify *de novo* a new medical device without device predicates into Class I or II without first requiring a "not substantially equivalent" determination under the 510(k) clearance process	Comparable to Senate provision	Comparable to Senate and House provisions
Regulation of mobile medical applications	Would prohibit the FDA from releasing final	Would not prohibit the FDA from releasing final	Comparable to House provision, except:

Issue	Original Senate-Approved Bill (S. 3187)	Original House-Approved Bill (H.R. 5651)	Final Enacted Law
	guidance on the regulation of mobile medical applications until it convenes a working group and drafts a report detailing a proposed strategy and recommendations for an "appropriate, risk-based regulatory framework" related to health information technology software	guidance on the regulation of mobile medical applications Would, however, require the FDA to draft a report that identifies strategies for coordinating the regulation of health information technology (including mobile medical devices) to avoid duplication, and that provides recommendations on an appropriate regulatory framework for health information technology, including a risk-based framework	• Modifies the draft report provision to require the FDA to draft a report that "contains a proposed strategy and recommendations on an appropriate, risk-based regulatory framework pertaining to health information technology, including mobile medical applications, that promotes innovation, protects patient safety and avoids regulatory duplication" (*i.e.*, similar to House requirement, but modifies required content of report)
510(k) medical device modifications	Would require the FDA to withdraw its controversial draft "Guidance for Industry and Staff—510(k) Device Modifications: Deciding When to Submit a 510(k) for a Change to an Existing Device" (issued July 27, 2011) Would also provide affected stakeholders the opportunity to comment before revised guidance on this issue is finalized	Comparable provision included in House bill (with regard to withdrawal of draft guidance only) Would also prohibit the FDA from issuing replacement draft guidance until its submission of a report to Congress on the applicability of 510(k) requirements for device modifications, and would prohibit finalization of replacement guidance until one year after issuance of the report Would also re-establish the effectiveness of the FDA's 1997 guidance "Deciding When to Submit a 510(k) for a Change to an Existing Device" until revised FDA guidance is issued (the FDA's draft guidance had proposed to replace the 1997 guidance as the FDA's "current thinking")	Comparable to House provision
FDA oversight of laboratory-developed tests	No comparable provision	Would require the FDA to give congressional committees 60 days' notice of the FDA's intent to issue	Comparable to House provision, except: • Adds statement that provision sunsets (ends)

Issue	Original Senate-Approved Bill (S. 3187)	Original House-Approved Bill (H.R. 5651)	Final Enacted Law
		draft or final guidance on the regulation of laboratory-developed tests, as well as the anticipated contents of such guidance	five years from the date of enactment
Drugs			
Registration of domestic and foreign drug establishments	Would expand the information required for establishment registration with the FDA to include the drug establishment's "unique facility identifier" and a point of contact's e-mail address	Would require drug establishments to include the unique facility identifier only	Comparable to Senate provision
Implementation of unique facility identifier system	Would authorize the FDA to "specify the unique facility identifier system"	Would require the FDA to (within two years of the bill's enactment) issue guidance specifying a unique facility identifier system	"Requires" the FDA to specify the unique facility identifier system"
Identifying drug establishments for inspection	Would require the FDA to use a risk-based system to identify drug establishments for inspection Relevant factors in assessing risk include compliance history of the establishment and the record, and history and nature of recalls linked to the establishment (among others)	Comparable to Senate provision	Comparable to Senate and House provisions
Effect of interference with FDA inspection of a drug establishment	No comparable provision	Would identify as "adulterated" any drug that has been manufactured, processed, packed or held in a factory, warehouse or establishment, if an agent of such location delays, denies, limits or refuses to permit an FDA inspection Would also require the FDA to (within one year) issue guidance that defines the circumstances under which an individual would be	Comparable to House provision

Issue	Original Senate-Approved Bill (S. 3187)	Original House-Approved Bill (H.R. 5651)	Final Enacted Law
		considered to be delaying, denying, limiting or refusing to permit an inspection	
Protection of confidential information provided to the FDA by a foreign government regulatory authority relating to a drug establishment	Would prohibit the FDA from disclosing—under the Freedom of Information Act (FOIA) or other laws—inspection-related information obtained from a foreign government regulatory authority if the information is provided or made available voluntarily on the condition that the information not be released to the public, and the information is covered by and subject to a certification by, and written agreement with, a foreign government	Comparable to Senate provision in terms of scope of information that may be protected by FOIA and the requirement for a written agreement However, would expand the exemption from FOIA to include drug-related information obtained from a federal, state, local or foreign government agency that has requested that the information be kept confidential	Comparable to Senate provision, except: • Restricts extent of FOIA protection from public disclosure information that concerns the inspection of a drug facility, is part of an investigation by the foreign government regulatory authority, alerts the United States to the potential need for an investigation, or concerns a drug that has a reasonable probability of causing serious adverse health consequences or death to humans or animals
Notice requirement for lost, stolen or counterfeit drugs	Would require two types of entities (a drug establishment or wholesale drug distributor) to notify the FDA in the event of "substantial loss or theft" of a drug, or if a drug has been or is being counterfeited and is in commerce in the United States or being offered for import into the United States	Would require a "regulated person" (*i.e.*, an establishment, commercial importer, wholesale distributor or any person who distributes drugs, except those who distribute exclusively for retail sale) to notify the FDA if the regulated person knows (1) that the use of such drug in the United States may cause "serious injury or death"; (2) of a "significant loss or known theft" of a drug intended for use in the United States; or (3) that a drug has been or is being counterfeited, and the product is in commerce or may reasonably be expected to be introduced into commerce, or the drug has been or is being imported into the United States, or may reasonably be expected to be offered for import into the United States	Comparable to House provision

Issue	Original Senate-Approved Bill (S. 3187)	Original House-Approved Bill (H.R. 5651)	Final Enacted Law
Disposition of adulterated, misbranded or counterfeit drugs offered for import	No comparable provision	Would permit the FDA to destroy, without opportunity for export, any drug refused admission into the United States that has a "reasonable probability of causing serious adverse health consequences or death" or is valued at $2,000 or less	Comparable to House provision, except: Would permit the FDA to destroy, without the opportunity for re-export, any adulterated, misbranded or counterfeit drug if such drug is valued at $2,500 or less
Penalty for drug adulteration	Significantly enhances penalty for "knowingly and intentionally" adulterating a drug in a manner that has a reasonable probability of causing serious adverse health consequences or death to up to 20 years' imprisonment and/or $1 million in fines (current maximum penalty for first violation is three years' imprisonment and/or $10,000 if committed with the intent to defraud or mislead)	Comparable to Senate provision	Comparable to Senate and House provisions
Penalty for drug adulteration	Significantly enhances penalty for "knowingly and intentionally" adulterating a drug in a manner that has a reasonable probability of causing serious adverse health consequences or death to up to 20 years' imprisonment and/or $1 million in fines (current maximum penalty for first violation is three years' imprisonment and/or $10,000 if committed with the intent to defraud or mislead)	Comparable to Senate provision	Comparable to Senate and House provisions
Penalties for drug counterfeiting	Significantly enhances penalty for an "individual" who "knowingly and intentionally" counterfeits drugs to up to 20 years' imprisonment and/or $4 million in fines for a first	Significantly enhances penalty for a "person" who knows or has reason to know that they are holding, selling or dispensing a counterfeit drug; potential penalties include fines or	Significantly enhances penalties, but enacts an entirely new provision based on the penalties in the U.S. Criminal Code for trafficking in (other) counterfeit goods and

Issue	Original Senate-Approved Bill (S. 3187)	Original House-Approved Bill (H.R. 5651)	Final Enacted Law
	offense; for subsequent offenses, penalties up to 20 years' imprisonment and/or $8 million in fines (current maximum penalty for first violation is three years' imprisonment and/or $10,000 if committed with the intent to defraud or mislead) Sets penalty for counterfeiting by a "person other than an individual" to up to $10 million for a first offense, and fines up to $20 million for subsequent offenses	imprisonment up to 20 years If use of a counterfeit drug is the proximate cause of a consumer's death, maximum penalty is life in prison	services (18 U.S.C. § 2320) • If an "individual" intentionally traffics counterfeit drugs, he or she could be fined up to $2 million and/or imprisoned up to 10 years for a first offense, and fined up to $5 million and imprisoned 20 years for a second or subsequent offense. • If a "person other than an individual" intentionally traffics counterfeit drugs, he or she could be fined up to $10 million for a first offense, and up to $15 million for a second or subsequent offense. • An individual that "knowingly or recklessly" causes or attempts to cause serious bodily injury through drug counterfeiting could be fined up to $5 million and/or imprisoned for up to 20 years; if committed by someone "other than an individual," the maximum fine is $15 million. • An individual that "knowingly or recklessly" causes or attempts to cause death through drug counterfeiting could be fined up to $5 million and/or imprisoned for life; if committed by someone "other than an individual," the maximum fine is $15 million.
Registration of commercial importers	No comparable provision	Would require a "commercial importer" of a drug to register with the FDA and to submit the unique facility identifier associated with the applicant's principal place	Comparable to House provision

Issue	Original Senate-Approved Bill (S. 3187)	Original House-Approved Bill (H.R. 5651)	Final Enacted Law
		of business Would deem a drug imported or offered for import by an unregistered commercial importer to be misbranded	
Documentation for admissibility of imports	Would permit the FDA to require, as a condition of granting admission to an imported drug or a drug offered for import, that the importer electronically submit certain documentation or information Would require the FDA to specify, by regulation, the information it will require, including (potentially) the regulatory status of the drug, unique facility identifier and indication of compliance with good manufacturing practices, among other information Would require the FDA to issue a final rule describing the required documentation within 18 months of the bill's enactment	Comparable provision in House bill (except would not require electronic submission of information, and would not provide a deadline for finalization of the associated regulation)	Comparable to Senate provision
"Track-and-trace" provisions	Would give the FDA authority to establish a uniform, comprehensive, national system to ensure the safety of the pharmaceutical supply chain Sponsoring senators had stated this provision was intended to serve "as a placeholder" while discussions continued on what would be the best structure for a national drug pedigree system to "trace back" a drug's chain of distribution without "preempting" more stringent state pedigree laws (*e.g.*,	No comparable provision	Provision not included in final bill Senate and House conferees were unable to reach agreement on the scope of a trace-back provision (*e.g.*, to drug lot or to drug unit).

Issue	Original Senate-Approved Bill (S. 3187)	Original House-Approved Bill (H.R. 5651)	Final Enacted Law
	those of California).		
Enhanced market exclusivity for qualifying anti-infective drugs	Would extend market exclusivity for a "qualified infectious disease product" by five years beyond the period to which the applicant is currently entitled under the Federal Food, Drug, and Cosmetic Act Would define "qualified infectious disease product" as an antibacterial or antifungal drug for human use intended to treat "serious or life-threatening infections" Designation as "qualified infectious disease product" may be made at any time before submission of a marketing application	Comparable extension of market exclusivity provision included in House bill However, would expand scope by defining "qualified infectious disease product" as an antibacterial or antifungal drug for human use that treats or prevents "an infection caused by a qualifying pathogen" Designation as "qualified infectious disease product" may be made at any time prior to submission of a marketing application, but no later than 45 days after submission of the application	Comparable to Senate provision
Expedited approval of drugs for serious or life-threatening diseases or conditions	Would allow the FDA to, at the sponsor's request, "facilitate the development and expedite the review" of a drug that is intended (either alone or in combination with another drug) for the treatment of a serious or life-threatening disease or condition, and that demonstrates the potential to address unmet medical needs for the disease or condition Current law only allows fast-tracking for serious or life-threatening conditions (not diseases), and does not provide that fast-track drug products may be used alone or in combination with other drugs	Comparable to Senate provision	Comparable to Senate and House provisions
Drug shortage: manufacturer notification to the FDA	Would require manufacturers of certain drugs (*i.e.*, drugs that are life supporting, life	Comparable to Senate provision, except: • Would also require notification from	Comparable to House provision, except: • Specifies that drugs intended for use in the

Issue	Original Senate-Approved Bill (S. 3187)	Original House-Approved Bill (H.R. 5651)	Final Enacted Law
	sustaining, intended for use in the prevention of a debilitating disease or condition, a sterile injectable product, or used in emergency medical care or during surgery—but not radiopharmaceuticals, human tissue replaced by a recombinant product, a product derived from human plasma or any other product designated by the FDA) to notify the FDA at least six months before taking action that would result in the permanent discontinuance of the manufacture of the drug, or that could lead to a meaningful interruption in the overall drug supply Permits the FDA to extend the notification requirement to biological products if the FDA determines that such requirement would benefit the public health	manufacturers of products intended for the "treatment" of a debilitating disease or condition (*i.e.*, would not be limited to drugs intended for "prevention") • Would not require notification from manufacturers of sterile injectable products or products used during emergency medical care or surgery • Exclusion from notification requirement would apply to radiopharmaceuticals, products derived from human plasma protein and their recombinant analogs, and any other product as designated by the FDA (*i.e.*, similar to the Senate provision, but slightly different scope of excluded products) • Would require manufacturers to provide the reason(s) for the discontinuance or interruption • Deletes provision that would have allowed the FDA to add certain biologics to the notification requirements	"prevention or treatment" of a medical condition—*i.e.*, drugs to which the notification requirement applies—include "any drug used in emergency medical care or surgery" • Limits the exclusion from notification requirement to radiopharmaceuticals and other products designated by the FDA (*i.e.*, deletes exclusion for human tissue replaced by a recombinant product and/or products derived from human plasma) • Adds language that allows the FDA to extend the notification requirement to biologics (*i.e.*, restores language from Senate bill); however, requires the FDA, in making the decision whether to extend the requirement to biologics, to consider whether there are any existing reporting programs and aim to reduce duplicative notification • Specifies that plasma products derived from human plasma protein and their recombinant analogs are among the biologics that could be added to the notification requirement (*i.e.*, gives the FDA flexibility to require or not require notification for these biological products)
Drug shortage: FDA consideration of enforcement action	Would affirmatively require the FDA to consider, before the issuance of an enforcement action, its effect on the availability of certain drugs (*e.g.*, drugs that are life supporting, life sustaining, intended for use	No comparable provision	Comparable to Senate provision, except: • Would only apply to drugs that are life supporting, life sustaining, or intended for use in the prevention or treatment of a debilitating

Issue	Original Senate-Approved Bill (S. 3187)	Original House-Approved Bill (H.R. 5651)	Final Enacted Law
	in the treatment of a debilitating disease or condition, a sterile injectable product, or used in emergency medical care or during surgery, but excluding products that are radiopharmaceuticals, human tissue replaced by a recombinant product, a product derived from human plasma or any other product designated by the FDA)		disease or condition—and would only exclude radiopharmaceuticals from its scope
Extension of period before forfeiting the 180-day marketing exclusivity period associated with an abbreviated new drug application (ANDA)	No comparable provision	Would give the first applicant to file a paragraph (iv) certification in connection with a generic drug marketing application up to 45 months from the date of filing the application to obtain tentative approval from the FDA before forfeiting the 180-day exclusivity period (current deadline to receive approval is 30 months from date of filing)	Comparable to House provision, except: • Only gives applicants up to 40 months from the date of filing to obtain tentative approval
Miscellaneous Provisions			
Internet promotion of FDA-regulated products	Would require the FDA (within two years of enactment of the bill) to issue guidance to industry describing its policy on the promotion of FDA-regulated products on the internet (including social media)	No comparable provision	Comparable to Senate provision
Impact of Risk Evaluation and Mitigation Strategies (REMS) on generic drug/biosimilar manufacturers	Would mandate that the element to ensure safe use in an REMS may not be used by brand name drug manufacturers to prohibit access to a drug or biological by a generic drug or biosimilar product developer	No comparable provision	Provision not included in final bill

Issue	Original Senate-Approved Bill (S. 3187)	Original House-Approved Bill (H.R. 5651)	Final Enacted Law
Deadline for agency action on citizen petition or petition for stay of agency action on a section 505(b)(2) application[2], an ANDA or a biosimilar application	No comparable provision	Would require the FDA to take final action within 150 days of receiving a citizen petition or a petition for stay of action on a 505(b)(2), ANDA or biosimilar application	Comparable to House provision
Public participation in agency activities	Would require the FDA to develop and implement strategies to solicit the views and perspectives of patients during product development and regulatory discussions	No comparable provision	Comparable to Senate provision
Scheduling of hydrocodone	Would delete language from current law that places doses and combinations of hydrocodone on DEA controlled substance schedule III—which has the effect of placing them in schedule II Would also add language keeping these drugs subject to penalties applicable to most schedule III drugs (Effect of law would be to require new prescriptions for refills, among other requirements)	No comparable provision	Requires the U.S. Department of Health and Human Services to hold a public meeting regarding the scheduling of hydrocodone within 60 days of enactment

Implications

Because the cost of reviewing marketing applications is, in large part, offset by the FDA's assessment of user fees, the failure to reauthorize the agency's power to charge user fees would have had serious consequences, including substantial additional delays in review time and fewer approvals. As a result, the enactment of the Food and Drug Administration Safety and Innovation Act marks a critical development in the effort to ensure that the FDA has the capacity to review drug, device and biological marketing applications in a timely yet scientifically appropriate fashion. The importance of the legislation is underscored by the nearly unanimous votes to pass the law and the fact that the legislation was passed prior to the Supreme Court of the United States' ruling on the Affordable Care Act (ACA)—which, among other things, eliminated the possibility for other health-care-reform-related amendments to the legislation, which could have delayed passage. The Supreme Court's June 28, 2012, ruling on the ACA also means that the biosimilar provisions and the medical device tax in the user fee legislation remain in effect.

[2] A 505(b)(2) application is a new drug application that contains full reports of investigations of safety and effectiveness, but in which some of the investigations relied upon for approval are those not conducted by or for the applicant and for which the applicant has not obtained a right of reference. *21 U.S.C. §355(b)(2).*

In addition to the user fee authorization/reauthorization, the legislation addresses (or requires the FDA to address) a number of hot-button regulatory issues, including the FDA's regulation of internet advertising for regulated products, laboratory-developed tests and mobile medical applications (among many others). However, the legislation's most notable non-user-fee development may be the inability to reach agreement on the implementation of a federal "track-and-trace" system for drugs. Faced with complex drug pedigree requirements at the state level (e.g., in California), drug manufacturers had hoped that the enactment of a federal standard and track-and-trace system would "preempt" or uniformly apply instead of many differing state requirements. However, congressional conferees were unable to agree on a standard, for example, whereby tracking would be performed at the drug lot level (preferred by manufacturers) compared to tracking at the drug unit level (preferred by the FDA). Notwithstanding this disagreement, it is expected that the implementation of a federal track-and-trace system will continue to be a topic of legislative, industry and FDA interest in the foreseeable future.

For more information, please contact your regular McDermott lawyer, or:

James S. Cohen: +1 202 756 8276 jscohen@mwe.com

Michael Ryan: +1 202 756 8088 mryan@mwe.com

For more information about McDermott Will & Emery visit www.mwe.com