FDA User Fees and the Regulation of Drugs, Biologics, and Devices: Comparative Analysis of S. 3187 and H.R. 5651

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Summary

UPDATE: On June 18, 2012, the Senate Committee on Health, Education, Labor, and Pensions and the House Committee on Energy and Commerce distributed the text of an agreement that combined provisions of S. 3187 [ES], as passed by the Senate on May 24, 2012, and H.R. 5651 [EH], as passed by the House on May 30, 2012. The full House passed the new version by voice vote under suspension of the rules on June 20, 2012. On June 25, 2012, the Senate voted for cloture to limit debate on that bill, S. 3187 [EAH], the Food and Drug Administration Safety and Innovation Act of 2012 [hereinafter referred to as "the agreement"]. The Senate is expected to vote on the agreement sometime the week of June 25, 2012. For information on selected features of the agreement, see the Introduction of this report.

The Senate Committee on Health, Education, Labor, and Pensions and the House Committee on Energy and Commerce have worked for more than a year developing Food and Drug Administration (FDA)-related legislation, versions of which both chambers passed in the last week of May 2012. S. 3187 (the Food and Drug Administration Safety and Innovation Act) and H.R. 5651 (the Food and Drug Administration Reform Act of 2012) each include provisions that would affect the regulation of human drugs, biological products, and medical devices, along with several agency-wide administrative or miscellaneous items. Majority and minority committee leaders have expressed the desire to get a completed bill to the President before July 4, 2012.

The impetus to the timing of these bills is that current authority for FDA to collect fees under the Prescription Drug User Fee Amendments (PDUFA) of 2007 and the Medical Device User Fee Amendments (MDUFA) of 2007 will expire on October 1, 2012, unless reauthorizing legislation is enacted before then. Member statements at committee hearings indicated no opposition to reauthorization and very little comment about changes to the current user fee programs. Because Members of Congress generally consider the user fee reauthorizations to be must-pass legislation—for example, the user fee revenue accounts for more than half of the agency's human drug program budget—they have used these bills as vehicles for numerous additional measures.

The introduction to this report highlights selected features of S. 3187 [EAH], the agreement, relative to S. 3187 [ES] and H.R. 5651 [EH]. The remainder of this report provides, in a series of 14 tables, comparisons of the provisions in S. 3187 [ES] and H.R. 5651 [EH], presented generally in the order in which they appear in the Senate bill, the first to be reported by committee. Each table addresses a broad topic (e.g., human device regulation) and is preceded by narrative discussing the policy and legislative context of the table's provisions.

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Introduction

Update on Senate-House Agreement, S. 3187 [EAH]

On June 18, 2012, the Senate Committee on Health, Education, Labor, and Pensions and the House Committee on Energy and Commerce distributed the text of an agreement that combined provisions of S. 3187 [ES], as passed by the Senate on May 24, 2012, and H.R. 5651 [EH], as passed by the House on May 30, 2012. The full House passed the new version by voice vote under suspension of the rules on June 20, 2012. On June 25, 2012, the Senate voted for cloture to limit debate on that bill, S. 3187 [EAH], the Food and Drug Administration Safety and Innovation Act of 2012 [hereinafter referred to as "the agreement"]. The Senate is expected to vote on the agreement sometime this week.

Selected features of the agreement are noted below, by major issue area (e.g., drug shortages). Bill references are to the Senate bill (S. 3187 [ES]), the House bill (H.R. 5651 [EH]), and the agreement (S. 3187 [EAH]). A notation at the end of each bullet directs readers to tables within the report that present provisions in S. 3187 [ES] and H.R. 5651 [EH].

• User fees. Titles I through IV cover the reauthorization of prescription drug and medical device user fees and the authorization of generic drug and biosimilar biological product user fees. Both the Senate and House bills were based on the Department of Health and Human Services-proposed legislative language. The agreement includes additional annual reporting requirements regarding generic drug and biosimilar biological product applications, based on a Senate bill provision; and additional reporting elements regarding prescription drug and medical device applications, based on House bill provisions. [Tables 1-4]

• Pediatric medical products. In general, the agreement adopts elements of both the Senate and the House bills. It adopts the House language requiring the Secretary to provide the rationale for pediatric study requests under the Best Pharmaceutical for Children Act that do not request studies in neonates. It also includes new language requiring the staff of the Office of Pediatric Therapeutics to include at least one individual with expertise in pediatric subpopulations that are less likely to be studied. The agreement does not include the Senate provision regarding pediatric labeling and clinical exclusivity. [Table 5]

• Human device regulation. The agreement omits Senate language that would have required the Secretary to develop a report on health information technology with input from a working group prior to the issuance of final guidance on medical mobile applications, while retaining the requirement that the Secretary develop the report; in addition, the agreement adopts the House language that would have required FDA to notify Congress prior to issuing guidance on the regulation of laboratory-developed tests (LDTs). [Table 6]

• Pharmaceutical supply chain. The agreement would provide the Secretary of Health and Human Services with several enhanced authorities and new responsibilities to assure drug safety, including: domestic and foreign facility registration requirements using unique identifiers; risk-based inspection frequency; administrative detention authority; and notification requirements, among others. The agreement does not include Senate-passed provisions regarding a supply chain security (track-and-trace) system, or third-party auditor accreditation. [Table 7]

• Antimicrobial incentives. The agreement adopts the Senate language defining a qualified infectious disease product—a product that would receive an extension of exclusivity and expedited review—as an antibacterial or antifungal drug for human use intended to treat serious or life-threatening infections. [Table 8]

• Expedited drug development and review. The agreement adopts the Senate language that would replace current statutory language addressing expedited drug development and review, including fast-track products, breakthrough therapies, and accelerated approval generally. [Table 9]

• Drug shortages. The agreement is a blend of the Senate and House drug shortage provisions and would require any manufacturer to notify the Secretary of both a permanent discontinuance and a manufacturing interruption that is likely to lead to meaningful disruption of the U.S. supply of that drug. It would explicitly authorize the Secretary to expedite establishment inspections and the review of supplements to applications to mitigate or prevent shortages. The agreement adopts the Senate language regarding a Secretarial task force and strategic plan, and House provisions regarding reports from the Comptroller General and the Attorney General and a drug shortage list to be maintained and made publicly available by the Secretary, unless doing so would conflict with trade secrets or would adversely affect the public's health. [Table 10]

• Marketing exclusivity. The agreement includes a modified House provision that would temporarily extend the period during which a manufacturer could obtain tentative approval of a first generic drug application before forfeiting marketing exclusivity. [Table 12]

• Petitions. The agreement includes a modified House provision regarding the timeframe during which the Secretary must take final agency action regarding various petitions. [Table 12]

• Risk Evaluation and Mitigation Strategies (REMS). The agreement includes a House provision to amend requirements and procedures concerning assessments of approved Risk Evaluation and Mitigation Strategies (REMS) and their modification. It does not include a Senate provision to prohibit a manufacturer from citing a REMS distribution restriction to limit the supply of a drug to a drug developer for testing purposes. [Table 12]

• Advisory committee conflicts of interest. The agreement generally adopts a House provision expanding recruitment efforts for potential advisory committee appointees and maintaining conflict of interest provisions while revising provisions on waivers and public disclosure of conflicts of interest. [Table 13]

• Hydrocodone. The agreement replaces Senate-passed language (which would have rescheduled hydrocodone in the Controlled Substances Act) with language that would require the Secretary, if practicable, to hold a public meeting and solicit stakeholder input regarding products containing hydrocodone. [Table 14]

• Selected miscellaneous provisions. The agreement would: establish a certification pathway for medical gases; require efforts to harmonize clinical trial standards among different countries; require FDA information technology and workforce strategies and plans; provide "whistleblower" protections to commissioned officers in the U.S. Public Health Service; and set compliance deadlines for sunscreen labeling regulations. The agreement does not include Senate provisions on tanning bed labeling or clinical trial registration. [Tables 12 and 14]

The Senate and the House have each passed bills whose provisions would affect a broad range of Food and Drug Administration (FDA) activities regarding drugs, biological products, and medical devices: S. 3187, the Food and Drug Administration Safety and Innovation Act, passed on May 24, 2012; and H.R. 5651, the Food and Drug Administration Reform Act of 2012, passed on May 30, 2012. The timing of these bills coincides with the October 1, 2012 expiration of FDA's authority under current law to collect fees under the Prescription Drug User Fee Amendments (PDUFA) of 2007 and the Medical Device User Fee Amendments (MDUFA) of 2007. Because revenue from those fees supports over 2,000 full-time equivalent FDA positions and accounts for more than half of the agency's drug and device review resources, Members of Congress have referred to the user fee reauthorizations as generally uncontroversial, must-pass legislation. The Senate Committee on Health, Education, Labor, and Pensions and the House Committee on Energy and Commerce have, in addition to developing legislation that would reauthorize the drug and device user fees, crafted additional titles that would create new user fee authority for generic drugs and biosimilar biological products, permanently authorize programs to encourage or require studies of drugs for pediatric use, medical device regulation, drug regulation, and several areas, such as advisory committee conflict of interest, that cut across FDA product areas. Congress had also made user fee authorizing legislation in 2007 a vehicle for addressing other FDA-related issues.[1]

This report provides a legislative analysis of the provisions in S. 3187 and H.R. 5651, including brief summaries of relevant provisions in current law, mostly the Federal Food, Drug, and Cosmetic Act (FFDCA). Current law descriptions generally relate only to provisions that the bills would change; the current law column, therefore, does not always provide a complete description of the relevant law. Material is grouped by broad topics and presented in the general order of sections in the Senate bill, the first to be reported out of committee. The report begins each topic

[1] The Food and Drug Administration Amendments Act of 2007 (FDAAA, P.L. 110-85) included, along with reauthorization of prescription drug and medical device user fee programs, provisions on drug safety, direct-to-consumer drug advertising, pediatric drugs and medical devices, clinical trial databases, the creation of a new nonprofit entity to assist FDA with its mission, and food safety.

with a discussion of the overall issue to set the policy or legislative context of the bills' provisions and then uses a table to present the comparison of the bills and current law.

In Tables 1 through 4, which describe the legislative language for four user fee programs, the Senate and House descriptions are merged in one column because of their substantive similarity (the few differences are noted). Tables 3, 4, and 11 address new provisions and do not, therefore, have current law columns. The remaining tables have three columns: current law, S. 3187, and H.R. 5651. In each table, the rows generally follow the order of provisions in the Senate bill, with comparable House provisions, if any, described in the relevant Senate rows. House provisions without comparable Senate provisions are then presented in the order they appear in the House bill.

The following grid lists the tables that follow in this report; it also lists the section numbers of S. 3187 (as passed) and H.R. 5651 (as passed) covered in each table.

Table Link and Topic Area	S. 3187 (as passed)	H.R. 5651 (as passed)
Table 1. Fees Relating to Drugs	Secs. 101-107	Secs. 101-107
Table 2. Fees Relating to Medical Devices	Secs. 201-208	Secs. 201-208
Table 3. Fees Relating to Generic Drugs	Secs. 301-307	Secs. 301-307
Table 4. Fees Relating to Biosimilar Biological Products	Secs. 401-407	Secs. 401-407
Table 5. Pediatric Medical Products	Secs. 501-511	Secs. 501-506, 751, 772, 865
Table 6. Human Device Regulation	Secs. 601-616	Secs. 601, 604, 701-705, 711-712, 721, 731-732, 741-742, 751, 761-762, 771, 773
Table 7. Pharmaceutical Supply Chain	Secs. 701-716, 722	Secs. 801-815
Table 8. Incentives for Anti-Infective Drugs	Secs. 801-806	Secs. 831-835
Table 9. Expedited Drug Development and Review Processes	Secs. 901-902	Secs. 841-843, 869
Table 10. Drug Shortages	Sec. 1001	Secs. 901-908
Table 11. Medical Gas Regulation	Secs. 1111-1113	Secs. 821-823
Table 12. Human Drug Regulation: Miscellaneous	Secs. 723, 903-908, 1101, 1124, 1131	Secs. 861-864, 866-868, 870
Table 13. Advisory Committee Conflicts of Interest	Sec. 1121	Sec. 602
Table 14. Administrative Reforms and Miscellaneous Provisions	Secs. 1102, 1122-1123, 1125-1130, 1132-1154	Secs. 603, 851

This report is one in a suite of CRS products that provide detailed background and analysis of FDA-related issues. For further information on many of the issues that Members and panelists raised in the committee hearings leading up to these bills (including drug approval, development incentives, device regulation, pediatric drugs, and user fees), see the CRS website (the Medical Product Regulation listings at http://www.crs.gov/pages/subissue.aspx?cliid=2678) or contact Susan Thaul, Specialist in Drug Safety and Effectiveness, or one of the other authors of this report.

User Fee Acts

Titles I through IV of both the Senate and House bills would authorize FDA to collect user fees and direct the revenue to fund specified activities relating to prescription drugs, medical devices, generic drugs, and biosimilar biological products. The first two are reauthorizations of current programs; the second two would authorize new user fee programs.

With the Prescription Drug User Fee Act in 1992, Congress authorized FDA to collect user fees from the manufacturers of brand-name prescription drugs and biological products and to use the revenue for specified activities.[2] PDUFA became possible when FDA, industry, and Congress agreed on two concepts: (1) *performance goals*—FDA would commit to performance goals it would negotiate with industry that set target completion times for various review processes; and (2) *use of fees*—the revenue from prescription drug user fees would be used only for activities to support the review of human drug applications and would supplement—rather than replace—funding that Congress appropriated to FDA. The added resources from user fees allowed FDA to increase staff to review what was then a backlog of new drug applications and to reduce application review times. Over the years, Congress has added similar authority regarding medical devices and animal drugs.[3] User fees make up 35% of the FY2012 FDA budget. Their contribution to FDA's human drug program is larger at 51%.[4]

Following the precedent set by PDUFA, all the user fee programs addressed in this legislation include both (1) legislation and (2) performance goals agreements developed with representatives of the regulated industry in consultation with representatives of patients and advocates, academic and science experts, and congressional committees.

Prescription Drug User Fee Reauthorization[5]

FDA may use the revenue from PDUFA fees to support "the process for the review of human drug applications."[6] With each reauthorization of PDUFA, Congress has expanded the range of activities included in that phrase. The prescription drug user fee program covers new drugs whose sponsors are the first to apply for marketing approval (excluding, therefore, generic drugs) and new biological products (excluding, therefore, the new category of biosimilar biological projects).

Material in **Table 1** refers to changes that S. 3187 (as passed) and H.R. 5651 (as passed) would make to current law. Unless otherwise noted, the PDUFA provisions in S. 3187, H.R. 5651, and the HHS-proposed legislative language are substantively the same. For a more complete

[2] The Prescription Drug User Fee Act (PDUFA) and its reauthorizations are in P.L. 102-571, P.L. 105-115, P.L. 107-188, and P.L. 110-85. For discussions of PDUFA, see CRS Report R42366, *Prescription Drug User Fee Act (PDUFA): Issues for Reauthorization (PDUFA V) in 2012*, and CRS Report RL33914, *The Prescription Drug User Fee Act: History Through the 2007 PDUFA IV Reauthorization*, both by Susan Thaul.

[3] The Medical Device User Fee Act (MDUFA) and its reauthorization are in P.L. 107-250 and P.L. 110-85. The Animal Drugs User Fee Act is in P.L. 108-130, and the Animal Generic Drugs User Fee Act is in P.L. 110-316. For discussions of these user fee programs, see CRS Report R42508, *The FDA Medical Device User Fee Program*, by Judith A. Johnson, and CRS Report RL34459, *Animal Drug User Fee Programs*, by Sarah A. Lister.

[4] CRS Report R41964, *Agriculture and Related Agencies: FY2012 Appropriations*, coordinated by Jim Monke.

[5] Susan Thaul, Specialist in Drug Safety and Effectiveness, prepared this section of the report.

[6] FFDCA Section 735(6) [21 USC 379g (6)]

description of current law and discussion of issues relating to the Prescription Drug User Fee Act, see CRS Report R42366, *Prescription Drug User Fee Act (PDUFA): Issues for Reauthorization (PDUFA V) in 2012*, by Susan Thaul.

Table 1. Fees Relating to Drugs

Current Law	S. 3187 (as passed) and H.R. 5651 (as passed)
Human drug application and supplement fee	
A human drug *application fee* is assessed for an application for which clinical data with respect to safety or effectiveness are required for approval. The fee for an application that does not require clinical data, or for a supplement, is half the application fee. The fee is due at the time of application or supplement submission. Exceptions are made for a previously filed application or supplement under certain conditions and for a designated orphan drug or indication. [FFDCA 736(a)(1); 21 USC 379h(a)(1)]	Would make technical changes only.
Prescription drug establishment fee	
A prescription drug *establishment fee* is assessed annually for each establishment listed as manufacturing the prescription drug product named in an approved human drug application. Exceptions apply to certain compounded positron emission tomography (PET) drugs and designated orphan products. [FFDCA 736(a)(2); 21 USC 379h(a)(2)]	Would make a technical change about date payable.
Prescription drug product fee	
A prescription drug *product fee* is assessed annually for each prescription drug product named in an application (except for a product whose manufacturer has had no pending application since September 1992). [FFDCA 736(a)(3); 21 USC 379h(a)(3)]	Would make a technical change about date payable.
Exceptions apply to specified products, including the same product as another product approved under an application filed under section 505(b) or 505(J). [FFDCA 736(a)(3); 21 USC 379h(a)(3)]	Would add that the referent product under FFDCA Section 505(b) or 505(j) is not on a list of discontinued products compiled under section 505(j)(7).
Fee revenue amounts	
The law established total prescription drug user fee revenues for each fiscal year, subject to specified adjustments. It requires that each fee type provide one-third of the total revenue. Total fee revenue for FY2008 was set at $392,783,000. [FFDCA 736(b)(1,2); 21 USC 379h(b)(1,2)]	Would set total fee revenue for FY2013 at $693,099,000. [The HHS-proposed legislative language, submitted to Congress on January 13, 2012, set total fee revenue for FY2013 at $712,808,000.]
A modified workload adjustment factor for FY2007 is specified that differed from that in effect for FY2006. [FFDCA 736(b)(3); 21 USC 379h(b)(3)]	Would replace FFDCA 736(b)(3) with a different formula to reflect changes made in FFDCA 736(c) [see below] for the FY2013 workload adjustment and would add an inflation adjustment for FY2013. The inflation adjustment and the workload adjustments would be calculated as described in FFDCA 736(c) [see below] beginning with $652,709,000.

Current Law	S. 3187 (as passed) and H.R. 5651 (as passed)
Additional fee revenues for drug safety	
PDUFA IV directed that, in addition to the adjusted revenue value based on $392,783,000, there be fee revenues collected and used for drug safety in specific amounts summing to $225 million from FY2008 through FY2012. [FFDCA 736(b)(4); 21 USC 379h(b)(4)]	No comparable provision.
Inflation adjustment	
The inflation adjustment is based on the greater of the Consumer Price Index (all U.S. urban) for the previous year; or the total percent change in the previous year in General Schedule basic pay, as adjusted by DC-area locality pay; [FFDCA 736(c)(1); 21 USC 379h(c)(1)]	Would add that inflation adjustment be a weighted average of the CPI figure and the FDA personnel cost figures, such that it is the sum of one plus— The CPI figure such that —the average annual change for the first 3 years of the preceding 4 years of available data; and —multiplied by the proportion of all costs other than personnel compensation and benefits costs to total costs of the process for the review of human drug applications (as defined in FFDCA Section 735(6)) for the first 3 years of the preceding 4 fiscal years.
Or,	**And,**
as added by PDUFA IV, the average change in annual cost per FTE FDA position of all personnel compensation and benefits for the first 5 of the preceding 6 fiscal years. [FFDCA 736(c)(1)]	Would calculate the FDA personnel cost such that it uses the first 3 of the preceding 4 fiscal years; multiplied by the proportion of personnel compensation and benefits costs to total costs of the process for the review of human drug applications for the first 3 years of the preceding 4 years.
Workload adjustment	
Fee revenues are adjusted to reflect changes in FDA's workload for the process for the review of human drug applications. The calculation was based on a weighted average of the change in the total number of human drug applications, commercial investigational new drug (IND) applications, efficacy supplements, and manufacturing supplements submitted. PDUFA IV added that (1) the calculation count commercial IND applications as the number that were active during the most-recent 12-month period for which data are available; (2) the number of human drug applications is adjusted for changes in review activities.	Would not allow the adjustment to result in fee revenues that are less than the totals established in FFDCA Sec. 736(b) as adjusted for inflation.
The adjustment for changes in review activities may not result in more than an additional 2% increase for 2009; and	No comparable provision.
(3) the Secretary must contract with an independent accounting firm to study the adjustment for changes in review activities and make any warranted recommendations. The Secretary may not make changes unless the study has been completed, and, once the study has been completed, must make any appropriate changes. [FFDCA 736(c)(2); 21 USC 379h(c)(2)]	Would refer to an independent accounting or consulting firm that would conduct periodic reviews and publish reports on the adequacy of the adjustment, including recommendations for change. The Secretary, after getting public comments, could change the methodology to be in effect the following fiscal year.

Current Law	S. 3187 (as passed) and H.R. 5651 (as passed)
Rent and rent-related cost adjustment	
PDUFA IV directed the Secretary to decrease (up to $11.7 million) the fee revenue total if actual costs paid for rent and rent-related expenses are less than estimates made for such year in FY2006. [FFDCA 736(c)(3); 21 USC 379h(c)(3)]	No comparable provision.
Final year adjustment	
The Secretary may increase total fee revenue if necessary to provide for up to three months of operating reserves for the process of human drug application review for the first three months following sunset.	Would not change current law.
PDUFA IV added that the final year adjustment may *decrease* fee revenue if FY2009 or FY2010 appropriations for both FDA and the review of human drug applications exceed the amounts appropriated for those activities for FY2008—a "reverse trigger." This decrease is limited to a maximum of $65 million. [FFDCA 736(c)(4)(B); 21 USC 379h(c)(4)(B)]	No comparable provision.
Crediting and availability of fees	
Each five-year authorization specifies the amount of prescription drug user fees authorized to be appropriated for each fiscal year, subject to specified adjustments. The amount of fees collected in excess of the amount specified in appropriations acts is to be (1) credited to FDA's appropriation account, and (2) subtracted from the amount that would otherwise have been authorized to be collected during subsequent fiscal years. PDUFA IV specified that the amount of excess collections is based on a cumulative calculation of fees collected in each year, and that the offset must be reflected in the amount authorized to be collected in the final year. [FFDCA 736(g); 21 USC 379h(g)]	The amount of fees authorized to be collected would be subject to any decisions made based on the independent report that would be required [see FFDCA Sec. 736(c) above]. Would add provision allowing the Secretary to accept early payment of authorized fees.
Performance reports	
The Secretary must submit an annual report concerning the progress FDA has made in achieving the goals outlined in the FDA-industry agreement. [FFDCA 736B(a); 21 USC 379h-2(a)]	Would require that the report also include future FDA plans for meeting the goals. The House provision would require that the report cover two additional items: (1) the status of the independent assessment required by this act, and (2) the progress, by review division, of the Center for Drug Evaluation and Research and the Center for Biologics Evaluation and Research in achieving goals, as specified in this section, as well as future plans for meeting the goals. [The HHS-proposed legislative language did not address FFDCA Sec. 736B.]

Source: CRS analysis of current law, S. 3187 (as passed), and H.R. 5651 (as passed).

Note: Section numbers in current law determined topic order in this table.

Medical Device User Fee Reauthorization[7]

Congress gave FDA the authority to collect fees from the medical device industry in 2002.[8] User fees and direct appropriations from Congress fund review of medical devices by the FDA. Medical devices are a wide range of products that are used to diagnose, treat, monitor, or prevent a disease or condition in a patient. For many medical devices, FDA approval or clearance must be obtained prior to marketing in the United States. The purpose of user fees is to support the FDA's medical device premarket review program and to help reduce the time it takes the agency to review and make decisions on marketing applications. The user fee law provides revenue for FDA; in conjunction, the agency negotiates with industry to set *performance goals* for the premarket review of medical devices. The medical device user fee program was modeled after PDUFA program.

Table 2 refers to changes in current law that would be made by Sections 202 and 203 of S. 3187 (as passed), and Sections 202 and 203 of H.R. 5651 (as passed). The language in these sections of the two bills is virtually identical. For a more complete description of the MDUFA program see CRS Report R42508, *The FDA Medical Device User Fee Program*, by Judith A. Johnson.

Table 2. Fees Relating to Medical Devices

Current Law	S. 3187 (as passed) and H.R. 5651 (as passed)
Definitions	
Provides definitions for a number of terms. [FFDCA 737; 21 USC 379i]	Would update the definition of "adjustment factor" and change the definition of "establishment subject to a registration fee." Note: this change would increase the number of establishments paying the fee from 16,000 to 22,000.
Types of fees	
A fee is assessed for: -premarket application (PMA); -premarket report, equal to the PMA fee; -panel track supplement, 75% of the PMA fee; -180-day supplement, 15% of the PMA fee; -real-time supplement, 7% of the PMA fee; -30-day notice, 1.6% of the PMA fee; -efficacy supplement, equal to the PMA fee; -premarket notification submission [510(k)], 1.84% of the PMA fee; -request for classification information, 1.35% of the PMA fee; and -periodic reporting concerning class III device, 3.5% of PMA fee. There are exceptions made for some devices. [FFDCA 738(a)(2)(A); 21 USC 379(j)]	Would set fee for 510(k) at 2% of the PMA fee.

[7] Judith A. Johnson, Specialist in Biomedical Policy, prepared this section of the report.

[8] MDUFMA (P.L. 107-250) added Sections 737 and 738 to the Federal Food, Drug and Cosmetic Act (FFDCA) [21 USC 379i and 379j]. MDUFMA was amended twice by the Medical Device Technical Corrections Act of 2004 (MDTCA; P.L. 108-214) and the Medical Device User Fee Stabilization Act of 2005 (MDUFSA; P.L. 109-43).

<table>
<tr><th>Current Law</th><th>S. 3187 (as passed) and
H.R. 5651 (as passed)</th></tr>
<tr><td colspan="2">Annual establishment registration fee</td></tr>
<tr><td>An establishment registration fee is assessed annually. Exceptions are made for an establishment operated by a state, federal, or Indian tribe unless the device is intended for commercial distribution. [FFDCA 738(a)(3); 21 USC 379(j)]</td><td>Would make a technical change to date payable.</td></tr>
<tr><td colspan="2">Premarket application (PMA) and establishment fee amounts</td></tr>
<tr><td>Fees are based on the following amounts which may be adjusted by the Secretary for various reasons:
<table><tr><th>PMA</th><th colspan="2">Establishment</th></tr><tr><td>FY2008</td><td>$185,000</td><td>$1,706</td></tr><tr><td>FY2009</td><td>$200,725</td><td>$1,851</td></tr><tr><td>FY2010</td><td>$217,787</td><td>$2,008</td></tr><tr><td>FY2011</td><td>$236,298</td><td>$2,179</td></tr><tr><td>FY2012</td><td>$256,384</td><td>$2,364</td></tr></table>[FFDCA 738(b); 21 USC 379(j)]</td><td>New FFDCA Sec. 738 (b)(1)-(2). Would change fee amounts and change reasons for adjustment:
<table><tr><th>PMA</th><th colspan="2">Establishment</th></tr><tr><td>FY2013</td><td>$248,000</td><td>$2,575</td></tr><tr><td>FY2014</td><td>$252,960</td><td>$3,200</td></tr><tr><td>FY2015</td><td>$258,019</td><td>$3,750</td></tr><tr><td>FY2016</td><td>$263,180</td><td>$3,872</td></tr><tr><td>FY2017</td><td>$268,443</td><td>$3,872</td></tr></table></td></tr>
<tr><td colspan="2">Total fee revenue amounts</td></tr>
<tr><td><table><tr><td>FY2008</td><td>$48,431,000</td></tr><tr><td>FY2009</td><td>$52,547,000</td></tr><tr><td>FY2010</td><td>$57,014,000</td></tr><tr><td>FY2011</td><td>$61,860,000</td></tr><tr><td>FY2012</td><td>$67,118,000</td></tr></table>[Was FFDCA 738(h); 21 USC 379(j)]</td><td>Total revenue amounts, new FFDCA Sec. 738 (b)(3). Would set total fee revenue amounts as follows:
<table><tr><td>FY2013</td><td>$97,722,301</td></tr><tr><td>FY2014</td><td>$112,580,497</td></tr><tr><td>FY2015</td><td>$125,767,107</td></tr><tr><td>FY2016</td><td>$129,339,949</td></tr><tr><td>FY2017</td><td>$130,184,348</td></tr></table></td></tr>
<tr><td colspan="2">Annual fee setting</td></tr>
<tr><td>The Secretary publishes fee amounts in the Federal Register 60 days before the start of each fiscal year. [FFDCA 738(c)(1); 21 USC 379(j)]</td><td>Secretary would, 60 days before the start of each fiscal year, establish fees based on amounts specified in subsection (b) and the adjustments in this subsection, and publish such fees and rationale for adjusting fee amounts in the Federal Register.</td></tr>
<tr><td colspan="2">Inflation adjustment</td></tr>
<tr><td>The Secretary may increase the establishment fee for FY2010 only if the estimate of the number of establishments submitting fees for FY2009 is less than 12,250. If the fee for FY2010 is adjusted, fees for FY2011 and FY2012 may be increased by 8.5% over the previous year. The determination and its rationale must be published in the Federal Register. [FFDCA 738(c)(2); 21 USC 379(j)]</td><td>Would adjust total revenue amounts by a specified inflation adjustment based on the sum of one plus—the average annual change in the cost per FTE position at FDA of all personnel compensation and benefits paid for the first 3 years of the preceding 4 fiscal years, multiplied by 0.60, and the average annual change in the Consumer Price Index (Metro DC, Baltimore, WV., not seasonally adjusted, all items, annual index) for the first 3 years of the preceding 4 years of available data multiplied by 0.40. If the base inflation adjustment for a fiscal year is less than 1, the adjustment is considered to be 1; or if it is greater than 1.04, the adjustment is considered to be 1.04. The base fee amounts in new subsection (b)(2) would</td></tr>
</table>

Current Law	S. 3187 (as passed) and H.R. 5651 (as passed)
	be adjusted as needed on a uniform proportional basis to generate the inflation adjusted total revenue amount.
Adjustment to establishment registration base fees	
No provision.	New FFDCA Sec. 738(c)(3). For each fiscal year, after the base fee amounts in new subsection (b)(2) are adjusted for inflation, the base establishment registration fee amounts would be further adjusted as necessary for total fee collections for the fiscal year to generate the total adjusted revenue amount.
Fee waiver or reduction	
No provision.	Would allow the Secretary to grant a waiver or reduced fees for a PMA or establishment fee if that is in the interest of public health. Waivers and fee reductions must be less than 2% of total fee revenue for that year. Authority for the waiver and reduced fees would end on October 1, 2017.
Conditions (Trigger)	
Direct appropriations must be more than 1% less than $205,720,000 multiplied by an adjustment factor, or else the Secretary may not collect user fees and is not required to meet performance goals. [FFDCA 738(g); 21 USC 379(j)]	Would change amount to $280,587,000.
Crediting and availability of fees	
Offset is handled as follows: the amount of fees collected, in the first three fiscal years and estimated for the fourth fiscal year, in excess of the amount specified in appropriations acts is credited to FDA's appropriation account, and the excess subtracted from the amount that would otherwise have been authorized to be collected during the fifth fiscal year. [FFDCA 738(h); 21 USC 379(j)]	Would add provision allowing the Secretary to accept early payment of authorized fees. Would authorize to be appropriated for FY2013 through FY2017 fees equal to the total revenue amount as specified under new subsection(b)(3), as adjusted for inflation and offset.
Streamlined hiring authority	
No provision.	New FFDCA Sec. 714 would allow the Secretary, without regard to provisions in title 5 USC, to appoint FDA employees to positions related to the process for the review of device applications in order to achieve the performance goals referred to in Sec. 738A(a)(1) as set forth in the Secretary's Commitment Letter. The authority to appoint such employees would terminate three years after the date of enactment.

Source: CRS analysis of current law, S. 3187 (as passed), and H.R. 5651 (as passed).

Generic Drug User Fee Authorization[9]

Material in **Table 3** refers to the legislation that would authorize the collection and use of generic drug user fees. The Generic Drug User Fee Amendments (GDUFA) titles in S. 3187 (as passed) and H.R. 5651 (as passed) would create new FFDCA sections 744A, B, C and are patterned after PDUFA, which was first enacted in 1992 and reauthorized in five-year increments. GDUFA would become effective October 1, 2012, or upon enactment, and would sunset on October 1, 2017. Unless otherwise noted, the GDUFA provisions in S. 3187, H.R. 5651, and the HHS-proposed legislative language are substantively the same.

Integral to the operation of the generic drug user program are the performance goals stated in the FDA-industry agreement that the HHS Secretary submitted to Congress along with proposed legislative language. For a description of that agreement and a discussion of issues relating the proposed Generic Drug User Fee Amendments of 2012, see CRS Report R42540, *Proposed FDA User Fee Acts: Generic Drug User Fee Amendments of 2012 (GDUFA) and Biosimilar User Fee Act of 2012 (BSUFA)*, by Susan Thaul and Judith A. Johnson.

Table 3. Fees Relating to Generic Drugs

(no current law)

S. 3187 (as passed) and H.R. 5651 (as passed)
Definitions
Would define the terms abbreviated new drug application, active pharmaceutical ingredient (API), adjustment factor, affiliate, facility, finished dosage form, generic drug submission, human generic drug activities, positron emission tomography drug, prior approval supplement, resources allocated for human generic drug activities, and Type II active pharmaceutical ingredient drug master file. [FFDCA 744A]
In particular, FFDCA Sec. 744A would define "human generic drug activities" as follows:
(8) Human generic drug activities means the following activities of the Secretary associated with generic drugs and inspection of facilities associated with generic drugs: (A) The activities necessary for the review of generic drug submissions, including review of drug master files referenced in such submissions. (B) The issuance of approval letters which approve abbreviated new drug applications or supplements to such applications or complete response letters which set forth in detail the specific deficiencies in such applications and, where appropriate, the actions necessary to place such applications in condition for approval. (C) The issuance of letters related to Type II active pharmaceutical drug master files which set forth in detail the specific deficiencies in such submissions and, where appropriate, the actions necessary to resolve those deficiencies or, if appropriate, document that no deficiencies need to be addressed. (D) Inspections related to generic drugs. (E) Monitoring of research conducted in connection with the review of generic drug submissions and drug master files. (F) Postmarket safety activities with respect to drugs approved under abbreviated new drug applications or supplements, including the following activities: (i) Collecting, developing, and reviewing safety information on approved drugs, including adverse event reports. (ii) Developing and using improved adverse-event data-collection systems, including information technology systems. (iii) Developing and using improved analytical tools to assess potential safety problems, including access to external data bases. (iv) Implementing and enforcing section 505(o) [21 USC § 355(o)] (relating to postapproval studies and

[9] Susan Thaul, Specialist in Drug Safety and Effectiveness, prepared this section of the report.

S. 3187 (as passed) and H.R. 5651 (as passed)

clinical trials and labeling changes) and section 505(p) [21 USC § 355(p)] (relating to risk evaluation and mitigation strategies) insofar as those activities relate to abbreviated new drug applications.
(v) Carrying out section 505(k)(5) [21 USC § 355(k)(5)] (relating to adverse event reports and postmarket safety activities).

(G) Regulatory science activities related to generic drugs.

Types of fees

GDUFA would establish three ongoing types of fees: drug master file (DMF); application filing (abbreviated new drug application (ANDA) and prior approval supplement (PAS)); and facility (generic drug (GDF) and active pharmaceutical ingredient (API)). It would also establish a one-time backlog fee. [FFDCA 744B(a)]

One-time backlog fee

Each person that owns a pending ANDA on October 1, 2012 (when GDUFA would become effective) that has not yet received tentative approval would be required to pay a one-time backlog fee.

Backlog fees would total $50 million divided by the number of pending ANDAs. [FFDCA 744B(a)(1)]

Drug master file fee

Each person that owns a Type II ("Drug Substance, Drug Substance Intermediate, and Material Used in Their Preparation, or Drug Product") active pharmaceutical ingredient (API) master file that is "referenced ... in a generic drug submission by any initial letter of authorization" would be required to pay a drug master file fee. This fee would be paid only the first time the drug master file is referenced.

This paragraph also includes requirements for (1) the Secretary to publish fees, (2) when the master file would be available for reference, and (3) fee due dates. [FFDCA 744B(a)(2)]

Abbreviated new drug application (ANDA) and prior approval supplement (PAS) filing fee

Each applicant that submits an ANDA would be required to pay a fee.

Each applicant that submits a prior approval supplement to an ANDA would be required to pay a fee.

This paragraph also includes requirements for (1) the Secretary to publish fees, (2) fee due dates, (3) refund conditions, (4) resubmission fees in specified circumstances, and (5) fee for API information not included by reference to Type II API drug master file. [FFDCA 744B(a)(3) and 744B(d)(3)]

Generic drug facility fee and active pharmaceutical ingredient (API) facility fee

Each person who owns a facility identified or intended to be identified in at least one approved or pending generic drug submission would be required to pay an annual fee.

Each person who owns a facility that produces or which is pending review to produce one or more APIs identified or intended to be identified in at least one approved or pending generic drug submission would be required to pay an annual fee.

Each person who owns a facility that meets both sets of criteria would be required to pay both fees.

This paragraph also includes requirements for (1) the Secretary to publish fees and (2) fee due dates. [FFDCA 744B(a)(4)]

Fee revenue amounts

The total estimated revenue for all fees for FY2013 would be $299 million, of which $50 million would be from the one-time backlog fee for pending applications. For each of FY2014 through FY2017, the total estimated revenue for the continuing fees would be $299 million.

Other than the one-time backlog fee, the relative proportion of each fee to the total annual amount would be:

S. 3187 (as passed) and H.R. 5651 (as passed)
6% from drug master file fees; 24% from ANDA and prior approval supplement fees; 56% from generic drug facility fees; and 14% from API facility fees. The fee for facilities located outside the United States would be $15,000-$30,000 higher than fees for facilities located in the United States, based on the difference in the cost of inspections as determined by the Secretary. [FFDCA 744B(b)]
Inflation adjustment
Each year, the Secretary would adjust the total revenues for inflation, as follows: The sum of one plus— the average percent change in the personnel compensation cost per full-time equivalent FDA position for the first three of the preceding four fiscal years multiplied by the proportion of such costs to total costs of human generic drug activities for those years; and the average percent change in the Consumer Price Index (CPI) for urban consumers in Washington-Baltimore, DC-MD-VA-WV for the first three years of the preceding four years of available data multiplied by the proportion of all costs other than personnel compensation and benefits to total costs of human generic drug activities for the first three years of the preceding four fiscal years. These adjustments would be added on a compounded basis each fiscal year. [FFDCA 744B(c)(1)]
Final year adjustment
The Secretary would be authorized to increase total fee revenue if necessary to provide for up to three months of operating reserves for the process of human generic drug activities for the first three months of FY2018 if adequate carryover balances are not available. [FFDCA 744B(c)(2)]
Annual fee setting
Based on revenue amounts established by the Act, the Secretary would be required to establish for FY2013: (1) by October 12, 2012, the one-time generic drug backlog fee for pending applications, the drug master file fee, the ANDA fee, and the prior approval supplement fee; and (2) within 45 days of the date to comply with the requirement for identification of facilities, the Secretary would be required to establish the generic drug facility fee and the API facility fee. The Secretary would be required to establish the various fees 60 days before the start of each fiscal year based on revenue amounts and adjustments provided in the Act. [FFDCA 744B(d)]
Limit
The total amount of fees charged, as adjusted under subsection (c), for a fiscal year may not exceed the total costs for such fiscal year for the resources allocated for human generic drug activities. [FFDCA 744B(e)]
Identification of facilities
The Secretary would be required, by October 1, 2012, to publish in the *Federal Register* a notice of the requirement to facility owners to identify certain facilities or sites. The owners would be required to comply within 60 calendar days of that notice. Each owner would be required to submit, update, or reconfirm the required information before June 1, 2013, and each subsequent fiscal year. The Secretary would specify the format and type of information required, which would include "identification of a facility identified or intended to be identified in an approved or pending generic drug submission." Other required

S. 3187 (as passed) and H.R. 5651 (as passed)
information includes whether the facility manufactures APIs and/or finished dosage forms and questions about its location, positron emission tomography drug manufacture, and whether it manufactures drugs that are not generic drugs. Any owner or operator of a site identified in a generic drug submission in which a bioanalytical study is conducted, or a clinical research organization, a contract analytical testing site, or a contract repackager site, would be required to provide ownership, name, and site address information to the Secretary, whose inspectional authority "shall extend to all such sites." [FFDCA 744B(f)]
Effect of failure to pay fees
This paragraph describes the effects of failure to pay fees that would be established by this section. Examples: the Secretary would not receive an ANDA from a person or affiliate of that person until that person pays the outstanding one-time backlog fee; and all drugs or APIs manufactured in a facility with an outstanding fee would be deemed misbranded. [FFDCA 744B(g)]
Limitations
If appropriations for FDA salaries and expenses for a fiscal year were not at least the amount for FY2009 excluding fees for that year, adjusted as described in this section, the fees must be refunded. The Secretary would be authorized to assess fees (other than the one-time backlog fees) after the start of a fiscal year rather than at its start. [FFDCA 744B(h)]
Crediting and availability of fees
This section would authorize fee collection and obligation only in the amount provided in advance in appropriations acts. Fees would remain available until expended and would be available only for human generic drug activities. The generic drug fees for a fiscal year after FY2012 would only be available if the Secretary allocates no less than $97 million, excluding fees and adjusted for inflation, for specified human generic drug activities. Compliance would include having a total up to 10% below that amount. Until enactment of a FY2013 appropriations act for FDA, FY2013 fees authorized by this section may be collected and credited. The Secretary would be authorized to accept early payment of authorized fees. This section would authorize to be appropriated for each of FY2013 through FY2017 fees according the total revenue amount and adjustments as specified in this section. [FFDCA 744B(i)]
Collection of unpaid fees
Any unpaid fee shall, after 30 days, be treated as a claim of the U.S. Government. [FFDCA 744B(j)]
Rule of construction
"This section may not be construed to require that" HHS reduce FTE positions of officers, employees, and advisory committee members in other areas to offset those "engaged in human generic drug activities." [FFDCA 744B(k)]
Positron emission tomography drugs
Fees upon application for a drug or an API and facility fees would not be required for a PET drug or an API for a PET drug. Such facilities would be required to comply with identification requirements. [FFDCA 744B(l)]
Disputes concerning fees
A person seeking return of a fee paid in error would be required to submit a written request to the Secretary within 180 calendar days after the fee was paid. [FFDCA 744B(m)]

S. 3187 (as passed) and H.R. 5651 (as passed)
Substantially complete applications
This paragraph would require an ANDA to "be deemed not to have been 'substantially complete'" if it is not received because of failure to pay an applicable fee. If the fee was the only reason, then when the fee is received, the application would be considered substantially complete and received. [FFDCA 744B(n)]
Annual performance and fiscal reports
The Secretary would be required to submit to the congressional committees annual performance and fiscal reports, and make them available to the public on the FDA website. [FFDCA 744C(a, b, c)] The House provision would require that the annual performance report also include specified regulatory science accountability metrics.
Consultation, public input and review, transmittal of recommendations, minutes of negotiation meetings
The Secretary would be required, in preparation for the reauthorization of GDUFA: –to consult with congressional committees, scientific and academic experts, health-care professionals, representatives of patient and consumer advocacy groups, and the generic drug industry to develop recommendations for GDUFA II, including goals and plans for meeting the goals; –before beginning reauthorization negotiations with the generic drug industry, to seek public input, including a *Federal Register* notice of a public hearing, a subsequent period for written comments from the public, and publication of those comments on the FDA website; –during negotiations with the generic drug industry, to hold at least monthly discussions with representation of patient and consumer advocacy groups; –after negotiations with the generic drug industry, to present recommendations to congressional committees, publish recommendations in the *Federal Register*, provide for a public comment period, hold a public meeting, and revise recommendations if necessary after considering such public views and comments; –to transmit the revised recommendations to Congress not later than January 15, 2017, including a summary of the public views and comments and any changes made in response to those views and comments; and –before presenting reauthorization recommendations to Congress, to make publicly available on the FDA website minutes of all negotiation meetings between FDA and the generic drug industry, including summaries of substantive proposals and significant controversies or differences of opinion and their resolution. [FFDCA 744C(d)]
Misbranding
This section would add a new subsection FFDCA section 502(aa) to consider misbranded a drug, an API, or a drug containing an API made in a facility for which fees have not been paid or identifying information that has not been submitted as required by this Act. [Sec. 306]
Streamlined hiring
This section would amend the new FFDCA Sec. 714 (as proposed in Sec. 208 of the bills) to authorize the Secretary to appoint employees to FDA positions without regard to competitive service provisions in USC Title 5 if their activities related to the process for the review of device applications (as defined in FFDCA Sec. 737) and human generic drug activities (as defined in the proposed new FFDCA Sec. 744A) according to related performance goals in FDA-industry agreements. [Sec. 307] This streamlined hiring authority would terminate 3 years after enactment. [Sec. 208]

Source: CRS analysis of S. 3187 (as passed) and H.R. 5651 (as passed).

Biosimilar User Fee Authorization[10]

A biosimilar is a biological product that is highly similar to a brand-name (innovator) biological product made by a pharmaceutical or biotechnology company.[11] A biological product, or biologic, is a preparation, such as a drug or a vaccine, that is made from living organisms. In contrast to the relatively simple structure and manufacture of chemical drugs, biosimilars, with their more complex nature and method of manufacture, will not be identical to the brand-name product, but may instead be shown to be highly similar.

The biotechnology industry began developing its first biologics for use as human therapeutic agents in the late 1970s and early 1980s. Biotechnology products are expected to become a larger share of the drugs sold by the pharmaceutical industry to U.S. consumers. However, with no parallel to the generic alternatives for chemical drugs, the cost of therapeutic biologics is often prohibitively high for individual patients.

Biological products are, in general, regulated—licensed for marketing—under the Public Health Service Act (PHSA), and chemical drugs are regulated—approved for marketing—under the Federal Food, Drug, and Cosmetic Act (FFDCA). The Drug Price Competition and Patent Term Restoration Act of 1984 (P.L. 98-417), often referred to as the Hatch-Waxman Act, provided a mechanism for the approval of generic drugs under the FFDCA but not under the PHSA.[12]

The Biologics Price Competition and Innovation Act of 2009 (BPCIA), enacted as Title VII of the Patient Protection and Affordable Care Act (ACA; P.L. 111-148), established a new regulatory authority within the FDA by creating a licensure pathway for biosimilars analogous to that which allowed for the approval of generic chemical drugs via the Hatch-Waxman Act. Under the new pathway, a biosimilar may be approved by demonstrating that it is highly similar to a biological product that is already allowed on the market by FDA. The BPCIA also authorized FDA to collect associated user fees.

The proposed Biosimilar User Fee Act (BSUFA) would require the collection of six types of fees from industry. Fee amounts would be based on inflation-adjusted PDUFA fee amounts for each fiscal year. Because there are no currently marketed biosimilar biological products, the proposal includes fees for products in the development phase to generate fee revenue for the new program and to enable companies to have meetings with FDA in the early development of biosimilar biological products. A company may chose to discontinue participation in the biosimilar biological product development program but must pay a reactivation fee to resume further product development with FDA.

The proposed legislative language would allow for the waiver of the biosimilar biological product application fee for the first such application from a small business. A "small business" is as an

[10] Judith A. Johnson, Specialist in Biomedical Policy, prepared this section of the report.

[11] There are no clinically meaningful differences between a biosimilar and the brand-name (also referred to as innovator) biological product in terms of the safety, purity, and potency of the product. Although a biosimilar or follow-on biologic is sometimes referred to as a biogeneric or generic biologic, the FDA and many others consider use of the word *generic* to be inaccurate because the term generic in the context of chemical drugs means identical and a biosimilar is not identical to the brand-name product. The FDA often uses the term *follow-on protein product*, because many biologics are proteins.

[12] For additional information about the Hatch-Waxman Act, see CRS Report R41114, *The Hatch-Waxman Act: A Quarter Century Later*, by Wendy H. Schacht and John R. Thomas.

entity with fewer than 500 employees, including affiliates, that does not have a drug product that has been approved under a human drug or biosimilar biological application and introduced or delivered for introduction into commerce. The biosimilars user fee authority would cease to be effective October 1, 2017. For further information, see CRS Report R42540, *Proposed FDA User Fee Acts: Generic Drug User Fee Amendments of 2012 (GDUFA) and Biosimilar User Fee Act of 2012 (BSUFA)*, by Susan Thaul and Judith A. Johnson.

Table 4 refers to changes that would be made by sections 402 and 403 of S. 3187 (as passed) and sections 402 and 403 of H.R. 5651(as passed); the language in the two bills is identical and differs from the HHS proposal in only minor technical details. These changes would add new sections 744G, 744H and 744I to the FFDCA.

Table 4. Fees Relating to Biosimilar Biological Products

(no current law)

S. 3187 (as passed) and H.R. 5651 (as passed)
Definitions
Provides definitions for a number of terms: adjustment factor, affiliate, biosimilar biological product, biosimilar biological product application, biosimilar biological product development meeting, biological product development program, biosimilar biological product establishment, biosimilar initial advisory meeting, costs of resources allocated for the process for the review of biosimilar biological product applications, final dosage form, financial hold, person, process for the review of biosimilar biological product applications, supplement. [FFDCA 744G]
Types of fees
Beginning in FY2013, the Secretary would be required to assess and collect several types of fees. [FFDCA 744H(a)]
Biosimilar development program fees
An *initial biosimilar biological product development program fee* would be assessed for submitting: a request for a biosimilar biological product development meeting, or an IND application to support a biosimilar biological product application. The fee would be due within 5 days after the request is granted or when the IND application is submitted, whichever is earlier. If an IND was submitted prior to enactment of BSUFA, this fee would be paid within 60 days of enactment or within 5 days after the request for a biosimilar biological product development meeting is granted. An *annual biosimilar biological product development program fee* would be assessed for each following fiscal year unless: a marketing application for the biological product was accepted for filing, or participation in the biosimilar biological product development program was discontinued. This fee would be due on the first business day of each fiscal year, or the first business day after enactment of an appropriations Act providing for the collection and obligation of such fees. Exceptions specified. Program participation could be discontinued if notification is submitted by August 1. If no IND application was submitted, written notification of discontinuation would be required. If an IND application were submitted, discontinuation would occur by withdrawing the IND application. If program participation were discontinued, a *reactivation fee* would be required to be paid by the earlier of the following: not later than 5 days after a request for a biosimilar biological product development meeting is granted, or when the IND application is submitted. A person who pays a reactivation fee would pay the annual biosimilar biological product development program fee beginning in the next fiscal year. If the initial, the annual, or the reactivation fee is not paid, the biosimilar biological product development meeting would not occur and, except under extraordinary circumstances, the IND application would not be received. Except under extraordinary circumstances, the sponsor of a clinical investigation would be prohibited from continuing the investigation (financial hold). Any biosimilar biological product application or supplement would be incomplete until all fees are paid. There would be no refunds, waivers, exemptions, or reductions of initial, annual, or reactivation fees. [FFDCA 744H(a)(1)]

S. 3187 (as passed) and H.R. 5651 (as passed)
Biosimilar biological product application and supplement fee
The fee for a *biosimilar biological product application* would be equal to the fee for a human drug application fee minus the cumulative amount paid for the following fees regarding the product named in the application: initial biosimilar biological product development program fee, annual biosimilar biological product development program fee, and any reactivation fee. If clinical data are not required, then the fee would be equal to 50% of the fee for a human drug application fee minus the cumulative amount paid for the following fees regarding the product named in the application: initial biosimilar biological product development program fee, annual biosimilar biological product development program fee, and any reactivation fee. The fee for a *supplement* for which clinical data are required would be equal to 50% of the fee for a human drug application fee. If a person pays an initial biosimilar biological product development program fee, annual biosimilar biological product development program fee, or a reactivation fee for a product before October 1, 2017, but submits a biosimilar biological product application after that date, the reduction of any biosimilar biological product application fee would still apply. Fees would be due upon submission of the application; exception applies for previously filed application or supplement that was not approved or was withdrawn. If application is refused for filing or is withdrawn, 75% of the fee would be refunded; the full fee would be required if resubmitted (unless the fee is waived for a small business). [FFDCA 744H(a)(2)]
Biosimilar biological product establishment fee
An establishment fee would be assessed for each establishment listed in an approved biosimilar biological product application that manufactures the biosimilar biological product named in the application. The establishment fee would be assessed in each fiscal year for which the biosimilar biological product fee would be assessed unless the establishment listed does not engage in the manufacture of the biosimilar biological product during the fiscal year. The fee is due the first business day of the fiscal year, or the first business day after enactment of an appropriations Act providing for the collection and obligation of such fees. Exceptions are specified. [FFDCA 744H(a)(3)]
Biosimilar biological product fee
An annual fee would be paid each fiscal year by the applicant named in the biosimilar biological product application. The fee is due the first business day of the fiscal year, or the first business day after enactment of an appropriations act providing for the collection and obligation of such fees. [FFDCA 744H(a)(4)]
Fee setting and amounts
The Secretary would, 60 days before the start of each fiscal year that begins after September 30, 2012, establish for the next year, the following fees based on the adjusted fee amount for each fiscal year as follows: -initial biosimilar biological product development program fee, 10% of human drug application fee; -annual biosimilar biological product development program fee, 10% of human drug application fee; -reactivation fee, 20% of human drug application fee; -biosimilar biological product application fee, equal to human drug application fee; -biosimilar biological product establishment fee, equal to prescription drug establishment fee; and -biosimilar biological product fee, equal to prescription drug product fee. For each fiscal year, the total amount of fees, as adjusted, would not be allowed to exceed the total costs for the resources allocated for the process for the review of biosimilar biological product applications. [FFDCA 744H(b)]
Application fee waiver for small business
Secretary would grant to the sponsor named in a biosimilar biological product application a waiver from the application fee for the first such application that a small business or its affiliate submits for review. A small business would be defined as an entity with less than 500 employees, including employees of affiliates, that does not have a drug product that has been approved under a human drug application (defined in FFDCA Sec. 735) or a biosimilar biological application (as would be defined in FFDCA Sec. 744G(4)) and introduced or delivered for introduction into interstate commerce. [FFDCA 744H(c)]

S. 3187 (as passed) and H.R. 5651 (as passed)
Effect of failure to pay fees
A biosimilar biological product application or supplement to which fees apply would not be considered to be complete and would not be accepted for filing until all fees are paid. [FFDCA 744H(d)]
Crediting and availability of fees
This section would authorize fee collection and obligation only in the amount provided in advance in appropriations acts. Fees would remain available until expended and would be available solely for the review of biosimilar biological product applications. The biosimilar fees for a fiscal year after FY2012 would only be available if the Secretary allocates no less than $20 million, excluding fees, adjusted. Would allow early payment of authorized fees. Would authorize to be appropriated for FY2013 through FY2017 fees equal to the total revenue amount as specified under subsection(b)(3), as adjusted for inflation and offset. [FFDCA 744H(e)]
Unpaid fees
An unpaid fee, after 30 days of the due date, would be treated as a claim of the U.S. Government. [FFDCA 744H(f)]
Written requests for waivers and refunds
A sponsor would be required to submit a written request to the Secretary for a waiver or a refund not later than 180 days after the fee is due. [FFDCA 744H(g)]
Rule of construction
"This section may not be construed to require that" HHS reduce FTE positions of officers, employees, and advisory committee members in other areas to offset those "engaged in the process of the review of biosimilar biological product applications." [FFDCA 744H(h)]
Performance report
Would require, beginning with FY2013, that the Secretary submit a report on the progress of FDA in achieving the performance goals during that fiscal year and future plans in meeting the goals each year to the House Committee on Energy and Commerce and the Senate Committee on Health, Education, Labor, and Pensions. [FFDCA 744I(a)]
Fiscal report
Would require, beginning with FY2013, that the Secretary submit a report on the use by FDA of the fees collected during that fiscal year each year to the House Committee on Energy and Commerce and the Senate Committee on Health, Education, Labor, and Pensions. [FFDCA 744I(b)]
Public availability
Performance and fiscal reports would be available on the FDA website. [FFDCA 744I(c)]
Study
Would require the Secretary to contract with a consulting firm to study the workload volume and full costs of the process for the review of biosimilar biological product applications; interim results would be published for public comment by June 1, 2015, and final results by the end of FY2016. [FFDCA 744I(d)]
Reauthorization
Would require the Secretary to consult with Congress, scientific and academic experts, health care professionals, patient and consumer advocacy groups, and the regulated industry in developing reauthorization recommendations for FY2013 through FY2017. Would require FDA, after negotiations with industry are completed, to present the recommendations to Congress, publish the recommendations in the *Federal Register*, provide a 30 day public comment period, hold a public meeting to receive views from the public, and revise the recommendations as necessary. Not later than January 15, 2017, the Secretary would be required to transmit to Congress the revised recommendations. [FFDCA 744I(e)]

Source: CRS analysis of S. 3187 (as passed) and H.R. 5651 (as passed).

Pediatric Medical Products[13]

Drug manufacturers may be reluctant to test drugs and medical devices in children because of economic, ethical, legal, and other obstacles.[14] Market forces alone do not provide sufficient incentives to overcome these obstacles. The Best Pharmaceuticals for Children Act (BPCA, P.L. 107-109) and the Pediatric Research Equity Act (PREA, P.L. 108-155) offer drug manufacturers financial and regulatory incentives to test their products for use in children. The Pediatric Medical Device Safety and Improvement Act of 2007 (PMDSIA, P.L. 110-85) creates reporting requirements for pediatric medical devices, incentives for manufacturers to create pediatric medical devices, and gives the FDA the authority to require postmarket studies of approved pediatric devices to ensure their continued efficacy and safety.

BPCA and PREA, passed by Congress in 2002 and 2003 and subsequently reauthorized in 2007, represent Congress' attempt to address the need for pediatric testing. BPCA created an incentive (extended market exclusivity) for manufacturers to conduct studies on pediatric use, and PREA created a requirement for manufacturers to test the safety and effectiveness of their products in pediatric populations. BPCA sunsets on October 1, 2012, and current law authorizes PREA only as long as BPCA is in effect.

Best Pharmaceuticals for Children Act

The FDA Modernization Act of 1997 (FDAMA, P.L. 105-115) provided an incentive in the form of a six-month extension of marketing exclusivity to drug manufacturers that completed pediatric studies requested by the FDA. The FDA would not approve the sale of another manufacturer's product during that period. In 2002, Congress passed the Best Pharmaceuticals for Children Act, which reauthorized this program for five years. In 2007, the FDA Amendments Act of 2007 (FDAAA, P.L. 110-85) reauthorized the program for another five years.

Extended marketing exclusivity may be an attractive incentive to a manufacturer with a product that is being sold under patent or other types of exclusivity protections.[15] BPCA also includes provisions to refer pediatric studies of off-patent products, which no longer have market exclusivity, to the National Institutes of Health (NIH), and manufacturer-declined studies of on-patent products to the Foundation for the NIH (FNIH).

Pediatric Research Equity Act

In 1998, FDA published a rule, known as the Pediatric Rule, which required manufacturers to submit pediatric testing data at the time of all new drug applications. In 2002, a federal court struck down the rule, holding that FDA lacked the statutory authority to promulgate it. Congress gave FDA that authority with PREA. PREA covers drugs and biological products and includes provisions for deferrals and waivers. Current law authorizes PREA only as long as BPCA is in effect.

BPCA and PREA studies result in information on new dosing, new indications of use, new safety information, and new data on effectiveness that inform labeling changes for pediatric dosing,

[13] Amalia K. Corby-Edwards, Analyst in Public Health and Epidemiology, and Susan Thaul, Specialist in Drug Safety and Effectiveness, prepared this section of the report. For follow-up discussions, contact Amalia Corby-Edwards.

[14] CRS Report RL33986, *FDA's Authority to Ensure That Drugs Prescribed to Children Are Safe and Effective*, by Susan Thaul.

[15] The FFDCA authorizes marketing exclusivity in specified circumstances for pediatric studies, orphan drugs, new chemicals, and patent challenges. FDA, "Frequently Asked Questions on Patents and Exclusivity," http://www.fda.gov/Drugs/DevelopmentApprovalProcess/ucm079031.htm.

warnings, and instructions on how to prepare formulations for pediatric populations. Although BPCA and PREA were developed separately, they are usually discussed in tandem. Their 2007 reauthorizations were paired in both committee hearings and legislative vehicle.

Both S. 3187 and H.R. 2516 would permanently authorize BPCA and PREA. They each would also amend or add provisions in current law. Provisions in these bills are compared with each other and to current law in **Table 5**.

Table 5. Pediatric Medical Products

Current Law	S. 3187 (as passed)	H.R. 5651 (as passed)
Authorization of BPCA and PREA		
BPCA is scheduled to sunset on October 1, 2012. PREA is authorized as long as BPCA is in effect. [FFDCA 505A(q); 21 USC 355a and FFDCA 505B(m); 21 USC 355c]	Would permanently authorize BPCA and PREA. [Sec. 501]	Similar to the Senate provision. [Sec. 501(b)(7) and Sec. 501(c)(9,10)]
Exclusivity		
In addition to the authority to grant pediatric market exclusivity regarding studies requested by the Secretary under BPCA, the Secretary may grant such exclusivity if completed studies required under other parts of the law are deemed to meet the criteria of this section. [FFDCA 505A(h); 21 USC 355a]	Would clarify the Secretary's authority to award exclusivity for studies conducted under PREA if they are completed and accepted pursuant to a written request under BPCA. [Sec. 502(a)]	Same as Senate provision. [Sec. 501(b)(2)]
The Public Health Service Act (PHSA) applies several provisions of BPCA (FFDCA Sec. 505A) to biological products licensed under the PHSA. [PHSA 351(m)(1); 42 USC 262(m)(1)]	Would add FFDCA Sec. 505A(h), re: eligibility of studies for exclusivity, and FFDCA Sec. 505A(n), regarding the referral of uncompleted studies to the Foundation for the National Institutes of Health and the pediatric program under PHSA 409I. [Sec. 502(b)]	Same as Senate provision. [Sec. 501(d)]
Pediatric Review Committee		
PREA 2007 established an internal review committee, referred to by the FDA as the Pediatric Review Committee (PeRC), with individuals in specified areas of expertise, to consult with reviewing divisions on pediatric plans and assessments for all applications, supplements, deferral and waiver requests that require a pediatric assessment under PREA and all written requests under BPCA. [FFDCA 505C; 21 USC 355d]	Would require the Secretary to issue internal standard operating procedures providing for PeRC review of any significant modifications made to initial pediatric study plans, agreed initial pediatric study plans, and written requests under PREA and BPCA. These internal standard operating procedures would be required to be publicly available on FDA's website. [Sec. 503]	Would add deferral extensions to the section title in the FFDCA regarding PeRC. It would also add neonatology to the list of required expertise on the PeRC. [Sec. 503]

Current Law	S. 3187 (as passed)	H.R. 5651 (as passed)
Adverse event reporting		
BPCA requires all adverse events in the one-year period following a labeling change to be referred to the Office of Pediatric Therapeutics for review by the Pediatric Advisory Committee. It also requires adverse event reports in subsequent years to be reported to the Office of Pediatric Therapeutics for review by the Pediatric Advisory Committee if deemed necessary. [FFDCA 505A(l); 21 USC 355a]	Would not change current law.	Would change the initial and subsequent time periods for reporting adverse events from one year to 18 months. It also provides assurances that nothing in this provision would prevent the Pediatric Advisory Committee from reviewing adverse event reports prior to the 18-month period if necessary. [Sec. 501(b)(3,4)]
Access to pharmacologic reviews		
PREA 2007 requires the public dissemination on the FDA website of the medical, statistical, and clinical pharmacology reviews of pediatric assessments no later than 210 days after submission. It also requires the dissemination of information regarding labeling changes resulting from pediatric assessments to physicians and other health care providers. [FFDCA 505B(h); 21 USC 355c] Note: There is no similar provision for requests under BPCA.	Would, within 3 years of enactment, extend the PREA requirement to studies submitted between January 4, 2002 and September 27, 2007 under BPCA that resulted in 6 months of market exclusivity and a labeling change. [Sec. 504]	Would provide an additional 110 days (no later than 330 days after the date of submission) for the publication of medical, statistical, and clinical pharmacology reviews of pediatric assessments required under PREA that do not receive priority review. [Sec. 501(c)(7)]
Deferrals and waivers		
Current law allows the Secretary to defer or waive the submission of some or all PREA-required assessments under specified circumstances. [FFDCA 505B(a)(3,4); 21 USC 355c]	Would allow the Secretary to extend a deferral of some or all required assessments if certain conditions are met and would require the applicant's annual report to the Secretary to include additional information, such as the projected completion date and the reason for the deferral. [Sec. 505(a)] Would also require the Secretary to annually aggregate the number of deferrals requested and granted, the timeline for completion of assessments, and the number of assessments completed and pending. [Sec. 505(b)]	Similar to Senate provision regarding extension of deferrals, but does not include the annual report additions. Would also provide that an assessment that has received a deferral shall not be considered late or delayed. [Sec. 501(c)(1)(B)] Would also clarify language regarding partial and full waivers. [Sec. 501(c)(1)(C)(i)]

Current Law	S. 3187 (as passed)	H.R. 5651 (as passed)
Tracking of deferrals and deferral extensions		
Current law requires the Secretary to track and make available to the public specified information on the assessments requested and completed under PREA. [FFDCA 505B(f)(6)(D); 21 USC 35c(f)(6)(D)]	Would add required information such as the number of postmarket noncompliance letters. [Sec. 505(c)]	Would require that the Secretary make the information available to the public not later than 60 days after it was submitted to the Secretary. [Sec. 501(c)(1)(B)(iii)]
Enforcement		
Current law allows a drug or biological product to be considered misbranded and subject to relevant enforcement action if a requested assessment is not submitted. [FFDCA 505B(d); 21 USC 355c]	Before considering a product to be misbranded based on this section, this provision would require the Secretary, according to specified timeframes, to issue a non-compliance letter to applicants who fail to submit their assessments, require a written response, and make the letter and response available to the public. [Sec. 505(c)]	Similar to the Senate provision, with different timeframes. [Sec. 501(c)(3)]
Pediatric study plans		
Current law requires the Secretary to meet with the sponsor of a new drug or biological product before and during the investigational process to discuss plans, timelines, and planned requests for waivers or deferrals of pediatric studies. [FFDCA 505B(e); 21 USC 355c] The Pediatric Review Committee (PeRC) is an FDA internal advisory committee. [FFDCA 505C; 21 USC 355d]	Would replace the current FFDCA Sec. 505B(e) with a provision on Pediatric Study Plans. This provision would require the Secretary and the applicant to take specific actions according to specified timeframes. Would require (a) the sponsor to submit an initial pediatric study plan, including description of the planned study or studies and indication of any planned deferral or waiver requests, prior to submission of the required pediatric assessments and 60 days after the end of the Phase II meeting *or such other equivalent time agreed upon between the Secretary and the applicant* (or earlier); (b) the Secretary to meet with the applicant within 90 days after receipt of the plan to discuss the plan or notify applicant that a meeting is not necessary and supply comments; (c) the applicant to submit an agreed pediatric study plan to the Secretary no later than 90 days after the meeting (or notification that a meeting is not necessary), which the Secretary would confirm; (d) the Secretary to consult the PeRC on the review of the initial pediatric study plan; the agreed pediatric study plan; and any	House provision is substantively the same as the Senate provision, except that it would require the Secretary to submit an initial pediatric study plan within 60 days after the end of the Phase II meeting *or at any other time as agreed upon by the Secretary and the applicant*. [Sec. 501(c)(4)]

Current Law	S. 3187 (as passed)	H.R. 5651 (as passed)
	significant amendments to such plans, which could be amended at any time; and (e) the Secretary to promulgate proposed regulations and issue proposed guidance to implement this pediatric study plans subsection within one year of enactment. Would specify that this pediatric study plan subsection take effect 180 days after enactment even if the Secretary has not promulgated regulations. [Sec. 506]	
Pediatric Advisory Committee		
The Pediatric Advisory Committee (PAC) was authorized to continue for a five-year period beginning on the date of enactment of BPCA of 2007. [P.L. 110-85, Sec. 502(d)]. The PAC advises on matters relating to pediatric research as specified. [P.L. 107-109, Sec. 14; P.L. 108-155, Sec. 3(b)(2); P.L. 110-85, Sec. 306(b); 42 USC 284m note]	Would permanently authorize the Pediatric Advisory Committee. [Sec. 507(a)]	Also would permanently authorize the Pediatric Advisory Committee, specifically regarding its responsibilities under FFDCA Secs. 505A, 505B, and 520(m), which are some, but not all, of the matters for which the PAC is currently responsible. [Sec. 505]
Pediatric Subcommittee of the Oncologic Drug Advisory Committee		
Current law authorizes the Pediatric Subcommittee of the Oncologic Drug Advisory Committee for a 5-year period beginning on the date of enactment of BPCA of 2007. [P.L. 107-109, Sec. 15; P.L. 110-85, Sec. 502(e); not codified]	Would reauthorize the Pediatric Subcommittee of the Oncologic Drug Advisory Committee (ODAC) in a manner consistent with the authorization of ODAC. [Sec. 507(b)]	Would delete the 2012 termination date, making the authorization permanent. [Sec. 506]
Humanitarian device exemption		
Current law authorizes the humanitarian device exemption (HDE) through FY2012. The HDE waives certain effectiveness requirements for devices meant to treat fewer than 4,000 individuals. It prohibits a manufacturer from making a profit on an HDE unless it is for pediatric use. [FFDCA 520(m)(6)(A)(iv); 21 USC 360j(m)(6)(A)(iv)] (The HDE is addressed more fully in **Table 6** of this report.)	Would extend the humanitarian device exemption to October 1, 2017. [Sec. 507(c)]	Also would extend the humanitarian device exemption to October 1, 2017. [Sec. 751(a)(1)]
Pediatric device availability demonstration grants		
Current law authorizes the Improving Pediatric Device Availability Demonstration	Would reauthorize the Improving Pediatric Device Availability Demonstration Grants through	Also would reauthorize the Improving Pediatric Device Availability Demonstration Grants through FY2017.

Current Law	S. 3187 (as passed)	H.R. 5651 (as passed)
Grants for $6 million for each of FY2008 through FY2012. [P.L. 110-85, Sec. 305(e); 42 USC 282 note]	FY2017. Would authorize the appropriation of $4.5 million for each of FY2013 through FY2017. [Sec. 507(d)]	[Sec. 772(b)] The House bill does not mention appropriations for this program.
Program for Pediatric Studies of Drugs		
The Program for Pediatric Studies of Drugs at NIH is authorized to publish and revise every 3 years a priority list of needs in pediatric therapeutics, including drugs, biological products, or indications, and authorizes funds for study of those issues. There are authorized to appropriated $200 million for FY2008 and such sums as are necessary for each of FY2009 through FY2012. [PHSA 409I(e)(1)(B); 42 USC 284m(e)(1)(B)]	Would authorize the appropriation of $25 million for each of FY2012 through FY2017. [Sec. 507(e)]	Would clarify the market exclusivity protections for drugs or biological products that must no longer apply in order for a drug to be studied for pediatric populations under this provision. Would authorize the appropriation of $25 million for each of FY2013 through FY2017. [Sec. 501(a)(3)]
Reports		
No provision.	Would require the Secretary to report to Congress 4 years after enactment and every 5 years thereafter that evaluates the effectiveness of BPCA and PREA in ensuring that medicines used by children are tested in pediatric populations and properly labeled for use in children. Specified required content would include detailed counts of various steps in the BPCA and PREA process. The Secretary must consult with stakeholders at least 180 days before the report is due regarding recommendations and suggestions regarding the effectiveness of the programs and possible changes to the programs. [Sec. 508]	The House provision is generally the same as the Senate provision. It specifies the content that would be required somewhat differently, and specifies that the report go to the Senate Committee on Health, Education, Labor, and Pensions, and the House Committee on Energy and Commerce, and be made available to the public. [Sec. 502]
Technical and conforming amendments, and transition rules		
Most BPCA and PREA provisions are codified in FFDCA Secs. 505A and 505B [21 USC 335a and 335c]	Would make several technical and conforming amendments to BPCA and PREA. [Secs. 506(b), 509]	Would make several technical and conforming amendments to BPCA and PREA. [Secs. 501(c)(5), 501(e), 501(f), 506]
Pediatric labeling and clinical investigation exclusivity		
FDA may provide a manufacturer 3 years of marketing exclusivity for a drug if the application or supplement to an application includes new clinical investigation regarding a new indication of an approved drug. Exclusivity may not be granted for studies not	Marketing exclusivity under FFDCA Sec. 505 would not apply to a pediatric study conducted under BPCA or PREA that results in labeling the product as not indicated for use in pediatric populations or subpopulations or that the study results were inconclusive or did not	Would not change current law.

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conducted by or for the applicant and if the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted. [FFDCA 505(c)(3)(E); 21 USC 355(c)(3)(E) and 505(j)(5)(F); 21 USC 355(j)(5)(F)]	demonstrate that the product is safe or effective in pediatric populations or subpopulations. Would amend both FFDCA Sec. 505A (BPCA) and, for clarity, FFDCA Sec. 505 (new drugs). Would reformat the provision in current law that describes the interaction of pediatric marketing exclusivity and generic drug marketing exclusivity [Sec. 510]	
Current law does not consider a generic drug application under FFDCA Sec. 505(j) ineligible for approval or misbranded solely because its labeling omits pediatric information that is protected by the patent or marketing exclusivity. [FFDCA 505A(o)(1,2); 21 USC 355a(o)(1,2)]	Would extend this provision to apply to other specified applications that rely on data not provided by the applicant. [Sec. 510(c)]	Would not change current law.
The Secretary may require labeling that omits the protected information to include "a statement of any appropriate pediatric contraindications, warnings, precautions, that the Secretary considers necessary." [FFDCA 505A(o)(2)(B); 21 USC 355a(o)(2)(B)]	Would not change current law.	Would amend the statement to end with "precautions, or other information that the Secretary considers necessary to assure safe use." [Sec. 501(b)(6)]
Rare pediatric disease priority review voucher incentive program		
No provision.	Would require the Secretary to hold a public meeting. within 18 months of enactment, to discuss ways to encourage and accelerate the development of new therapies for rare pediatric diseases. Would also require the Secretary to issue a strategic plan for encouraging and accelerating the development of new therapies for rare pediatric diseases within 180 days of the meeting. [Sec. 511]	Would create a new program to provide priority review vouchers for sponsors who create a new drug or biological product for a rare pediatric disease. The voucher would be awarded upon approval of the rare pediatric disease product application. It would be transferable (including by sale) to another sponsor. The program would terminate 1 year after the Secretary awards the third rare pediatric disease priority voucher under this section. Would require the Secretary to establish a user fee program for priority review vouchers. Would also provide the Secretary with the authority to designate a new drug as a drug for a rare pediatric disease. Applicants would need to provide the Secretary a description of their plan for marketing the rare disease product, and provide a post-approval production report within 5 years. If the rare pediatric disease product for which the voucher is

Current Law	S. 3187 (as passed)	H.R. 5651 (as passed)
		awarded is not marketed in the United States within 365 days of approval, the Secretary could revoke the priority review voucher. Would require the Secretary to report to Congress on the use of the priority review vouchers under specified circumstances. Would also require the GAO report on the effectiveness of awarding rare pediatric disease priority vouchers after the Secretary awards the third rare pediatric disease priority voucher. [Sec. 865]
Biosimilar biological products		
The NIH director may submit a proposed pediatric study request for a generic drug. [PHSA 409I(c)(1)(A)(i); 42 USC 284m(c)(1)(A)(i)]	Would not change current law.	Would add biosimilar biological products with approved applications under PHSA Sec. 351(k). [Sec. 501(a)(1,2)]
Studies in neonates		
Current law authorizes the Secretary to issue a request for pediatric studies under BPCA. [FFDCA 505A; 21 USC 355a]	Would not change current law.	Would amend current law to require the Secretary to include a statement describing the rationale for not requesting studies in neonates in the BPCA request for pediatric studies, if such a request is not made. [Sec. 501(b)(1)]
Pediatric studies		
Subsection "Referral if Pediatric Studies Not Completed" describes when the Secretary must refer requested studies to the Foundation for NIH or the pediatric study program at NIH [FFDCA 505A(n); 21 USC 355a(n)]	Would not change current law.	Would change subsection title to "Referral if Pediatric Studies Not Submitted" and extend the provision to include biosimilar biological products. [Sec. 501(b)(5)]
Requirement for PREA pediatric assessment when application holder declines a BPCA request		
After providing written notice that the holder of an approved new drug application declines a written request under BPCA that the Secretary did not refer to FNIH (under FFDCA Sec. 505A(n)), the Secretary may require the sponsor or holder to submit pediatric assessments if the Secretary finds certain criteria are met. [FFDCA 505B(b)(1); 21 USC 355c(b)(1)]	Would not change current law.	Would delete the requirement (in FFDCA Sec. 505B(b) regarding marketed products) that the Secretary first provides notice in the form of a letter. [Sec. 501(c)(1)(C)(2)]

Current Law	S. 3187 (as passed)	H.R. 5651 (as passed)
Labeling changes		
Current law allows 180 days after an application or supplement to an application for the Commissioner and the sponsor to resolve disagreements on labeling changes. [FFDCA 505B(g); 21 USC 355c]	Would not change current law.	Would provide the Commissioner and the sponsor 180 days to resolve labeling change disagreements for a product that received a priority review, and 330 days for a product that received a standard review. [Sec. 501(c)(6)]
Office of Pediatric Therapeutics		
Current law requires an Office of Pediatric Therapeutics in the FDA, with employees with specified areas of expertise, to coordinate and facilitate all FDA activities that affect pediatric populations. [FFDCA 1003a; 21 USC 393a(c)]	Would not change current law.	Would add neonatology and pediatric epidemiology to the areas of expertise required on the staff of the Office of Pediatric Therapeutics. [Sec. 504]
Final rule relating to tracking of pediatric uses of devices		
Current law requires an application, supplement to an application, or product development protocol for a new pediatric device to include certain information, including a description of the pediatric subpopulations that suffer from the condition the device is intended to treat, diagnose, or cure, and the number of pediatric patients. [FFDCA Sec. 515A(a)(2); 21 USC 360e-1(a)(2)]	Would not change current law.	Would require the Secretary to issue a proposed rule implementing the tracking of the information required by FFDCA Sec. 515A(a)(2) by December 31, 2012, and a final rule no later than December 31, 2013. [Sec. 772(a)]
Public meeting on pediatric cancers		
No provision.	No provision.	Would require the Secretary to hold a public meeting by December 31, 2013 on the impact of BPCA and PREA on the development of new therapies for children with cancer. [Sec. 501(g)]

Source: CRS analysis of current law, S. 3187 (as passed), and H.R. 5651 (as passed).

Human Medical Device Regulation[16]

Medical devices include a wide range of products that are used to diagnose, treat, monitor, or prevent a disease or condition in a patient. Medical devices are broadly integrated into health care, and include simple devices, such as tongue depressors, as well as more complex devices, such as implantable hips. The extent of FDA authority to regulate whether a device may be marketed in the United States and how it is monitored afterward varies across types of devices.[17]

In order to determine the applicability of premarket requirements (i.e., clearance or approval before marketing) for a given device, FDA classifies the device based on the risk to the patient: (1) low-risk devices are Class I; (2) moderate-risk are Class II; and (3) high-risk are Class III. Low-risk medical devices (Class I) and a very small number of moderate-risk medical devices (Class II) are exempt from premarket review. In general, for moderate-risk and high-risk medical devices, there are two pathways that manufacturers can use to bring such devices to market with FDA's permission: (1) premarket approval (PMA) and (2) premarket notification submission (also known as a 510(k) submission, after the section in the FFDCA that authorized this type of notification). According to a 2009 GAO report, of the more than 50,000 devices that were listed by manufacturers with FDA from FY2003 through FY2007, about 67% were exempt from premarket review; the remainder entered the market via the 510(k) process (31%), the PMA process (1%) or via other means, such as humanitarian use devices.[18]

Once a device is on the market, FDA has authority to carry out certain activities to monitor their safety and effectiveness. The extent of the agency's postmarket authority is tied to characteristics of the device. Manufacturer requirements include areas such as labeling, postmarket surveillance, device tracking, and adverse event reporting.

Provisions in the House and Senate passed bills both would make modifications to various aspects of premarket and postmarket device regulation. Premarket modifications include those intended to: (1) streamline the *de novo* 510(k) for novel devices; (2) affect the efficiency, transparency, and data requirements of the 510(k) and PMA processes; and (3) alter or make clarifications to certain types of exempt devices, for example, custom devices and humanitarian use devices. With respect to postmarket regulation, provisions focus on expanding active postmarket surveillance; altering requirements related to postmarket studies for devices; and strengthening both device recall and tracking capabilities through a recall program and the unique device identifier system. Miscellaneous reforms include those aimed at increasing transparency of FDA's approval and clearance decisions and processes for issuing industry guidance documents; improving health information technology for the agency; and harmonizing device regulation with FDA's international counterparts. Medical device related provisions are presented in **Table 6**, in the order in which they appear in the Senate bill.

[16] Amanda K. Sarata, Specialist in Health Policy; Judith A. Johnson, Specialist in Biomedical Policy; and Vanessa K. Burrows, Legislative Attorney prepared this section of the report. For follow-up discussions, contact Judith Johnson.

[17] For additional information, see CRS Report R42130, *FDA Regulation of Medical Devices*, by Judith A. Johnson.

[18] Government Accountability Office, *Medical Devices: FDA should take steps to ensure that high-risk device types are approved through the most stringent premarket review process*, GAO-09-190, January 2009, p. 9.

Table 6. Human Device Regulation

Current Law	S. 3187 (as passed)	H.R. 5651 (as passed)
Reclassification procedures		
The Secretary may, by regulation, change a device's classification based on new information and revoke, because of this change, any regulation or requirement under FFDCA Sec. 514 (performance standards) or Sec. 515 (premarket approval). The Secretary may obtain from the device classification panel a recommendation on the proposed classification change and must publish in the *Federal Register* any recommendation made by the panel about such change. A regulation changing the classification from class III to class II may provide that such classification will not take effect until the effective date of a performance standard for such device. [FFDCA 513(e); 21 USC 360c]	Would amend current law to allow the Secretary to change the classification of a device based on new information, and to revoke any regulation or requirement under FFDCA Secs. 514 or 515, by *administrative order instead of by regulation*. Would require publication of the proposed and final orders, public comment, and a meeting of a device classification panel. Administrative Procedure Act requirements regarding regulations would not apply, although the order would be subject to judicial review. An order changing the classification from class III to class II may provide that such classification will not take effect until the effective date of a performance standard for such device. The Secretary would be allowed to delegate the authority to issue the order to the FDA Commissioner, but such power could not be redelegated. The Commissioner would be required to issue an order proposed by the CDRH Director unless the Commissioner, in consultation with the Office of the Secretary, finds either that the order exceeds FDA's legal authority or would be lawful, but unlikely to advance public health. [Sec. 601]	Would not change current law.
Condition of approval studies		
The Secretary has the authority to attach a condition of approval to any order of approval for a PMA for a device. Specifically, the Secretary may require that the sale and distribution of the device be restricted, as specified. [FFDCA 515(d)(1)(B)(ii); 21 USC 360e(d)(1)(B)(ii)]	Would allow the Secretary, when issuing an order approving a premarket approval application, to require, as a condition of such approval, that the applicant conduct a postmarket study regarding the medical device. [Sec. 602]	Would not change current law.
Postmarket surveillance		
The Secretary is authorized to require manufacturers to conduct postmarket surveillance for any Class II or III device, if (1) the failure of the device would be reasonably likely to have serious adverse health consequences or (2) if the device is intended to be implanted in the body for more than one year or is life-	Would clarify that the Secretary may carry out this order either at the time of approval or clearance, *or at anytime thereafter*; and that the manufacturer would be required to commence the postmarket surveillance not later than 15 months after being so ordered. [Sec. 603]	Would not change current law.

Current Law	S. 3187 (as passed)	H.R. 5651 (as passed)
supporting and used outside of a device user facility. Such requirement may be ordered as a condition of either approval or clearance of a device. [FFDCA 522; 21 USC 360l]		
Sentinel		
Manufacturers of devices are broadly required to meet a number of requirements, as established by the Secretary, to assure that devices are not adulterated or misbranded and to otherwise assure their safety and effectiveness. These include, for example, device tracking and reports of removals and corrections, among others. [FFDCA 519; 21 USC 360i] In addition, the Secretary is required to establish a postmarket risk identification and analysis system (called Sentinel) for approved drugs, and to establish and maintain a number of procedures as part of this system, as specified. [FFDCA 505(k)(3)(C); 21 USC 355(k)(3)(C)(i)]	Would require the Secretary to modify Sentinel to include medical devices. Would clarify that private sector health-related electronic data used to carry out active adverse event surveillance would be allowed to include medical device utilization data, procedure and device registries, and claims data with respect to devices. The Secretary would be required, when expanding this system, to engage stakeholders and to use relevant data on cleared and approved devices, for example, patient survey data. [Sec. 604]	This section is comparable to the Senate provision. Unlike the Senate section, this section would strike a requirement that the Secretary establish and maintain procedures for the standardized reporting of data on all serious adverse drug events as part of Sentinel. [Sec. 762]
Recalls		
If the Secretary finds that there is a reasonable probability that a device intended for human use would cause serious, adverse health consequences or death, she must issue an order for an appropriate person to cease distribution and to notify health professionals and other device users. The Secretary must also issue an order to recall such device, according to specified processes. [FFDCA 513(e); 21 USC 360h(e)] Device recall audit checks are not defined in the FFDCA or in FDA regulations, although the FDA regulation for a person who is named in a cease distribution and notification order for a medical device contains language about effectiveness checks. However, general "recall audit checks" are defined in the FDA's Regulatory Procedures Manual: "A recall audit check is a personal visit, telephone call, letter, or a combination thereof, to a consignee of a recalling firm, or a user or consumer in the chain of distribution.	Would require the Secretary to create a program to assess information submitted pursuant to device recalls and information required to be reported regarding the removal or correction of a device. The Secretary would have to use this information to identify "strategies for mitigating health risks presented by defective or unsafe devices." The program would have to identify "trends in the number and types of device recalls," the types of most frequently recalled devices, and the causes of the recalls. Would also require the Secretary to clarify procedures for conducting device recall audit checks to improve consistency in the investigators' ability to perform those checks. It further would require the Secretary to develop explicit criteria for assessing whether an effective correction or removal action has been performed and to document the basis for the FDA's termination of a recall and certain correction or removal actions. [Sec. 605]	This section is comparable to the Senate section; it would add a new FFDCA section to establish a device recall program. Would require the Secretary to create a program to assess information on device recalls and use this information to proactively identify strategies for mitigating health risks presented by defective or unsafe devices. The program would have to identify trends in the number and types of device recalls, the most frequently recalled devices, and the underlying causes of the recalls. The section would also require the Secretary to clarify procedures for conducting device recall audit checks to improve consistency in the performance of those checks. It would further require the development of detailed criteria for assessing whether an effective correction or action plan for the recall has been performed, and documentation of the basis for the FDA's termination of a recall. Recall is defined for purposes of this new section. [Sec. 712]

Current Law	S. 3187 (as passed)	H.R. 5651 (as passed)
It is made to verify all consignees at the recall depth specified by the strategy have received notification about the recall and have taken appropriate action."		
Investigational device exemptions (IDEs)		
An Investigational Device Exemption (IDE) allows an unapproved device (most commonly an invasive or life-sustaining device) to be used in a clinical study to collect the data required to support a PMA application. PMA approval is based on a determination by FDA that the application contains sufficient valid scientific evidence to assure that the device is safe and effective for its intended use(s). All clinical evaluations of investigational devices (unless exempt) must have an IDE before the study is initiated. Devices are exempt from IDE requirements when testing is noninvasive, does not require invasive sampling, does not introduce energy into a subject, and is not stand alone (i.e., is not used for diagnosis without confirmation by other methods or medically established procedures). The IDE permits a device to be shipped lawfully for investigation of the device without requiring that the manufacturer comply with other requirements of the FFDCA, such as registration and listing. [FFDCA 520(g); 21 USC 360j, and 21 CFR 812]	Would allow the Secretary, at any time, to issue a clinical hold prohibiting the sponsor of a medical device from conducting a clinical investigation using the medical device if the Secretary determines the device represents an unreasonable risk to the safety of the persons who are the subjects of the clinical investigation or for such other reasons the Secretary may establish by regulation. The Secretary would make such a determination in writing, and would be able to take into account the qualifications of the clinical investigators, information about the device, the design of the investigation, the condition for which the device is intended, or the health status of the subjects. A written request by the sponsor for the removal of a clinical hold would receive a written decision within 30 days of receipt of the request. [Sec. 606]	Would not change current law.
Unique device identifier		
The Secretary is required to promulgate regulations establishing a unique device identification system. This system requires devices to bear a unique identifier, which serves to identify the device through both distribution and use. [FFDCA 519(f); 21 USC 360i(f)]	Would amend current law to require the Secretary to issue proposed regulations not later than December 31, 2012; to finalize the proposed regulations no later than 6 months after the close of the comment period; and to implement the final regulations with respect to certain devices, specifically those that are implantable, life-saving, and life sustaining, no later than 2 years after finalization of the regulations. [Sec. 607]	Would require the Secretary to promulgate regulations establishing a unique device identification system *not later than 120 days after enactment.* [Sec. 761]
Clarification of least burdensome standard		
For PMA applications, the Secretary, if requested, must meet with the applicant to determine the type of	Would clarify, for PMA applications, that the requirement for necessary clinical data means the minimum	This section is the same as the Senate section. [Sec. 702]

Current Law	S. 3187 (as passed)	H.R. 5651 (as passed)
valid scientific evidence, from one or more well-controlled clinical investigations, necessary to demonstrate the effectiveness of the device for the proposed conditions of use. The Secretary must consider, in consultation with the applicant, the least burdensome appropriate means of evaluating device effectiveness that would have a reasonable likelihood of resulting approval. [FFDCA 513(a); 21 USC 360c] For 510(k) notifications, when the Secretary requests information to demonstrate that devices with differing technological characteristics are substantially equivalent, only such information that is necessary to make substantial equivalence determinations may be requested, and the Secretary must consider the least burdensome means of demonstrating substantial equivalence and request information accordingly. [FFDCA 513(i); 21 USC 360c]	required to demonstrate, for purposes of approval, the effectiveness of a device for the conditions of use; this would not alter the criteria for evaluating a PMA application. Would also clarify, for 510(k) notifications, that the requirement for necessary information (to demonstrate that devices with differing technological characteristics are substantially equivalent) means the minimum required to support a determination of substantial equivalence between a new device and a predicate device; this would not alter the standard for determining substantial equivalence. [Sec. 608]	
Custom devices		
Devices which necessarily deviate from an otherwise applicable performance standard or requirement are not required to meet the requirements of FFDCA Sec. 514 (performance standards) or Sec. 515 (premarket approval). This applies to devices that are not generally available, as specified, and which are intended for use by a specific patient and made for that patient; which meet the needs of a physician or dentist in the course of professional practice; and which are not generally available to other physicians or dentists. [FFDCA 520(b); 21 USC 360j]	Would amend current law regarding the characteristics of devices that would be exempt from the requirements of Secs. 514 and 515. Would specify 3 additional characteristics of exempt devices: (1) those designed to treat a unique pathology or condition that no other device is domestically available to treat; (2) those assembled from components or manufactured and finished on a case-by-case basis; and (3) those with a common design, composition, and manufacture as commercially distributed devices. Would limit this exemption to devices: (1) that have the purpose of treating a sufficiently rare condition; (2) production of which is limited to no more than 5 units per year; and (3) whose manufacturers notify the Secretary on an annual basis of the manufacture of such device. Would require the Secretary to issue final guidance on replication of multiple devices (i.e., no more than 5 per year). Would not apply to oral facial devices. [Sec. 609]	This section is nearly identical to the Senate section. It would not exclude oral facial devices from the exemption from the requirements of FFDCA Secs. 514 and 515; in addition, it would not include the limitation requiring manufacturers to notify the Secretary on an annual basis of the manufacture of a device described under this section. [Sec. 771]

Current Law	S. 3187 (as passed)	H.R. 5651 (as passed)
Agency documentation and review of decisions regarding devices		
No provision.	Would add a new FFDCA Sec. 517A requiring the Secretary to provide a substantive written summary of the scientific and regulatory rationale for a decision to deny clearance of a 510(k) notification, deny approval of a PMA application, or disapprove of an IDE application. Within 30 day of receiving such a denial, the recipient may request a supervisory review of the denial decision. The Secretary, if so requested, would be required to schedule an in-person or teleconference review within 30 days after a request for review is made, and would be required to issue a decision to the person requesting a review not later than 45 days after the request for review was made, or 30 days after the in-person meeting or teleconference. This timeframe for review would not apply if consultation with experts outside the FDA is necessary, or if the sponsor introduces evidence not already in the administrative record. [Sec. 610]	This section is comparable but not identical to the Senate section. It would add a new FFDCA Sec. 517A requiring the Secretary to completely document the scientific and regulatory rationale for any significant decision regarding submission or review of a report under section 510(k), a PMA application or an IDE application, including documentation of significant controversies or differences of opinion. If requested, the Secretary would have to provide the applicant or person who submitted a 510(k) with such complete documentation. Within 30 day of such a decision, a person may request a supervisory review of the decision. The Secretary, if so requested, would be required to schedule an in-person or teleconference review within 30 days after a request for review is made, and would be required to issue a decision to the person requesting a review not later than 45 days after the request for review was made, or 30 days after the in-person meeting or teleconference. This timeframe for review would not apply if consultation with experts outside the FDA is necessary. [Sec. 703]
Good guidance practices relating to devices		
The Secretary is required to ensure public comment before the implementation of certain guidance documents, specifically those that set forth: (1) initial interpretations of a statute or regulation; (2) changes in interpretation or policy that are of more than a minor nature; (3) complex scientific issues; or (4) highly controversial issues. These four types of guidance documents are known as "Level 1 guidance documents" in FDA regulations. FDA regulations provide that for Level 1 guidance documents, the FDA "can seek or accept early input" before preparing a draft guidance document, and that FDA will both issue a *Federal Register* notice that the draft is available and post it online. The	Would treat the following notices related to devices as guidance documents for the purposes of ensuring that detailed procedural requirements pertaining to public participation (FFDCA Sec. 701(h)(1)(C); 21 C.F.R. 10.115(c)(1), (g)) would apply to such documents (unless the Secretary determines participation is not feasible or appropriate) before they could be implemented: (1) notice to industry guidance letters; (2) notice to industry advisory letters; and (3) notices setting forth either initial interpretations of a regulation or policy or changes in interpretation or policy. [Sec. 611]	Would modify the Secretary's obligations and discretion with regard to public comment; require additional procedures for the four types of guidance documents; and impact FDA regulations on review of existing guidance documents. It would specify that, with respect to devices, notice to industry guidance letters; notice to industry advisory letters; and similar notices that fall into the four types of guidance documents discussed under current law are to be treated as guidance documents subject to its provisions. Several guidance documents would not be treated as subject to these provisions for the four types of guidance documents: those that do not set forth an initial interpretation

Current Law	S. 3187 (as passed)	H.R. 5651 (as passed)
FDA then invites comments and may also hold public meetings or ask an advisory committee to review the guidance document. After receiving comments, FDA regulations provide that the agency will "incorporate suggested changes, when appropriate," into the final version of the guidance document, publish it both online and in the *Federal Register*, and implement the final guidance. The current FFDCA provision and regulation provide that if the Secretary determines that public participation "is not feasible or appropriate," the Secretary must provide for public comment "upon implementation and take such comment into account," revising the guidance "when appropriate." [FFDCA 701(h); 21 USC 371, and 21 CFR 10.115]		or reinterpretation of a statute or regulation; those that set forth changes in policy relating to internal FDA procedures; and agency reports, general information documents provided to consumers and health professionals, speeches, journal articles and editorials, media interviews, press materials, warning letters, memoranda of understanding, or communications directed to individual persons or firms. A minimum of 30 days before issuing one of the four types of draft guidance documents, the Secretary would be required to publish a notice in the *Federal Register*. The Secretary may meet with stakeholders and solicit public comment during preparation and before issuance of one of these four types of guidance documents. The Secretary would be allowed to waive the notice requirement and the option of meeting with the stakeholders and soliciting public comment if the Secretary upon a good cause finding that compliance with the notice and comment provisions was impracticable, unnecessary, or contrary to the public interest. The Secretary would be required to publish a good cause finding and reasoning in the *Federal Register*. Then, in the 90-day period after the date of the guidance document's issuance, the Secretary may meet with stakeholders and must take public comment. The Secretary would be required to indicate whether the guidance document draft issued is draft or final and finalize a draft within 18 months of its issuance, following the procedures above. The Secretary would be allowed to extend this deadline for issuing final guidance by up to 180 days and must submit a notification of extension in the *Federal Register*. If the Secretary did not finalize the draft within 18 months of its proposal (or the extension of that time), the Secretary would be required to treat the draft as null and void.

Current Law	S. 3187 (as passed)	H.R. 5651 (as passed)
		The Secretary would be required to review final guidance documents within five years after they are issued (under these new procedures) to ensure that the guidance is not outmoded, ineffective, insufficient, or excessively burdensome, and to accordingly modify, streamline, expand, or repeal such final guidance documents based on her review. [Sec. 601]
Modification of de novo application process		
FFDCA Sec. 513(f)(2) addresses the reclassification of certain devices that are automatically classified, by statute, as class III devices. This provision, added by FDAMA of 1997, is known as the "Evaluation of Automatic Class III Designation" or "De Novo Classification Process." It allows FDA to reclassify a novel low to moderate risk device into class I or II. Such a device would have automatically been classified into class III because, without a predicate device, FDA had found it to be not substantially equivalent (NSE) to a legally marketed device. Currently, a person who submits a report under Sec. 510(k) (premarket notification) for a type of device that has not been previously classified, that is classified into class III, may request that the Secretary classify the device into class I or II. The law specifies deadlines for such requests and for the Secretary's response. [FFDCA 513(f)(2); 21 USC 360c]	Would allow the Secretary to classify certain new devices without first issuing a determination that such devices are NSE to existing devices after reviewing a 510(k) submission. A person would be allowed to submit a request for initial classification of a device, and if the person declares that there is no legally marketed device upon which to base a substantial equivalence determination, the Secretary would be authorized to classify the device (into class I, II, or III) based on risk classification criteria. The person submitting the request would be permitted to recommend a classification, and if recommending class II, would be required to include a draft proposal for special controls that are necessary, along with general controls, to provide reasonable assurance of safety and effectiveness and a description of how the special controls provide such assurance. Such requests would be subject to electronic copy requirements. The Secretary could decline this classification request if there were in existence a legally marketed device on which to base a substantial equivalence review, or if the device was not a low-moderate risk device or that general controls would be inadequate to control risks and special controls cannot be developed. This section would lengthen the deadlines for action by the Secretary in response to a request and would require, within 2 years, a GAO report on the effectiveness of the review pathway under FFDCA Sec. 513(f)(2)(A), as amended by this section. [Sec. 612]	This section is comparable to, but not identical with, the Senate section. There would be no requirement for electronic copy submission. The Secretary would be allowed to decline this classification request if there were in existence a legally marketed device on which to base a substantial equivalence review, or if the device was not a low-moderate risk device or special controls cannot be developed. This section does not include a requirement for a GAO report. [Sec. 721]

Current Law	S. 3187 (as passed)	H.R. 5651 (as passed)
Humanitarian device exemptions (HDE)		
Device manufacturers may apply for an HDE, which exempts devices that meet certain criteria from the effectiveness requirements of premarket approval. HDE approvals are "based on evidence of safety and probable benefit." The Secretary must find that the device is intended to treat or diagnose a disease or condition that affects less than 4,000 people in the United States; the device would not be available to a person with the disease or condition unless an HDE was granted and that there is no comparable device available to treat or diagnose the disease or condition; and the device will not expose patients to an unreasonable or significant risk of illness or injury and that the benefit to health outweighs the risk of injury or illness from use of the device. Except for pediatric devices, HDE devices may not be sold for an amount that exceeds costs. A person may petition the Secretary to modify the annual distribution number for pediatric patients, but the number cannot exceed the number needed to treat 4,000 individuals. [FFDCA 520(m); 21 USC 360(m)]	Would amend the conditions that a device granted an HDE must meet in order to qualify for an exemption to the general ban on selling such devices for an amount that exceeds the costs of research, development, fabrication, and distribution (i.e., profit). A device would qualify for the exemption from the prohibition on profit if it were intended for the treatment or diagnosis of: (1) a disease or condition that *does not occur in pediatric patients*, or (2) that occurs in pediatric patients in such numbers that device development is impossible, highly impracticable, or unsafe. A person would be allowed to petition the Secretary to modify the annual distribution number and the Secretary could modify that number. The section would allow a sponsor of a device granted an HDE prior to the bill's enactment to seek a determination as to whether it would qualify for the exemption to the prohibition on profit and would require a GAO report on the impact of these modifications. [Sec. 613]	The House section is almost identical to the Senate section except as noted below. The House bill would strike from current law the provision allowing a manufacturer to petition the Secretary to modify the annual distribution number. [Sec. 751]
Reauthorization of third-party review		
Accredited persons may review 510(k) reports and make recommendations regarding the initial classification of devices. In general, accredited persons may not be used to review: a class III device; a class II device intended to be permanently implanted or life sustaining or life supporting; a class II device which requires clinical data in the report submitted under section 510(k). [FFDCA 523; 21 USC 360m]	Would reauthorize through October 1, 2017, the review of 510(k) submissions by accredited third parties. [Sec. 614]	This section is comparable to the Senate section. However, it would add a new subparagraph on periodic reaccreditation. Accreditation would be valid for 3 years. Requests for reaccreditation would be approved or denied by the Secretary within 60 days. Criteria on reaccreditation, and its denial, would be published in the *Federal Register* within 120 days of enactment. Reaccreditation would specify the activities and devices for which such persons are reaccredited. [Sec. 741]
Reauthorization of third-party inspections		
Accredited persons may conduct inspections of establishments that manufacture, prepare or process class II or class III devices. [FFDCA 704(g); 21 USC 374]	Would reauthorize through October 1, 2017, the inspection of a factory, warehouse, or manufacturing or processing establishment by accredited third parties. [Sec. 614]	This section is the same as the Senate section. [Sec. 742]

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Such inspections are required at least once in the 2-year period after registration and at least once in every successive 2-year period thereafter. [FFDCA 510(h); 21 USC 360]		
510(k) device modifications		
On January 10, 1997, the FDA issued final guidance, "Deciding When to Submit a 510(k) for a Change to an Existing Device." The guidance provides manufacturers direction on when to submit a 510(k) for a change to an existing device; specifically, it provides information clarifying the regulatory standard for this decision, that is, what is meant by major changes in intended use, as well as changes that could significantly affect the safety and effectiveness of the device. [21 CFR 807.81(a)(3)]	Would require the Secretary to withdraw the FDA guidance entitled "Guidance for Industry and FDA Staff—510(k) Device Modifications: Deciding When to Submit a 510(k) for a Change to an Existing Device." Before any future such guidance is issued, stakeholders would be provided with an opportunity to comment. [Sec. 615]	This section is comparable to the Senate section. It would require the Secretary to withdraw the same guidance. In addition, it would require, within 18 months of enactment, a report to the House Committee on Energy and Commerce and the Senate Committee on Health, Education, Labor, and Pensions regarding when a 510(k) should be submitted for a modification or change to a legally marketed device. The report would contain the interpretation of several specified terms. Draft guidance would not be issued before these committees receive the required report and final guidance would not be issued until one year after the committees receive such report. Prior guidance issued in 1997 would be in effect in the interim. [Sec. 705]
Health information technology		
Health information technology (HIT) is not defined in the FFDCA, but is defined in PHSA Sec. 3000(5), and includes technologies such as electronic health records, mobile medical applications, computerized health care provider order entry systems, and clinical decision support. PHSA Title XXX provides for the development of HIT standards; incentives for adoption of HIT by healthcare providers; and expansions of health information privacy and security protections. [PHSA 3000; 42 USC 300jj]	Would prohibit the Secretary from issuing final guidance on medical mobile applications without first meeting specified requirements relating to reporting and establishing a working group. Specifically, the Secretary would be required, within 18 months of enactment, to report to Congress on strategy and recommendations for a risk-based regulatory framework on medical device regulation and HIT software, including mobile applications, that promotes innovation and protects patient safety. In developing the report, the Secretary would be required to consult with the FDA Commissioner, the National Coordinator for Health Information Technology, and the Chairman of the Federal Communications Commission. In addition, in carrying out the reporting requirement, the Secretary would be required to convene a working group of external	Would require the Secretary, within 18 months of enactment, to report to Congress on coordinating federal regulation of HIT to avoid unnecessary duplication, including recommendations for a risk-based regulatory framework. In developing the report, the Secretary would be required to consult with the FDA Commissioner, the National Coordinator for Health Information Technology, and the Chairman of the Federal Communications Commission. [Sec. 773]

Current Law	S. 3187 (as passed)	H.R. 5651 (as passed)
	stakeholders and experts to provide input on the strategy. Federal Advisory Committee Act (FACA) requirements would apply to this group; FFDCA advisory committee requirements would not. [Sec. 616]	
FDA regulation of laboratory-developed tests (LDTs)		
FDA has the authority to ensure that LDTs are safe and effective for their intended use, as it does with all medical devices. Traditionally, the FDA has exercised its enforcement discretion in this area, choosing not to exercise enforcement authority over LDTs. However, the agency has regulated components of LDTs; for example, Analyte Specific Reagents (ASRs). [21 CFR 809.3, and FFDCA 201(h); 21 USC 321]	Would not change current law.	Would prohibit the FDA from issuing any draft or final guidance on the regulation of LDTs without notifying, at least 60 days in advance, the House Committee on Energy and Commerce and the Senate Committee on Health, Education, Labor, and Pensions, of its intention to do so and the details of such action. [Sec. 604]
Investigational device exemptions		
FFDCA Sec. 520(g) requires the Secretary, in a manner specified, to establish procedures for the investigational use of uncleared devices, i.e., the investigational device exemption (IDE). The statute states that the purpose of FFDCA Sec. 520(g) is "to encourage to the extent consistent with the protection of the public health and safety and with ethical standards, the discovery and development of useful devices intended for human use and to that end to maintain optimum freedom for scientific investigators in their pursuit of that purpose." [FFDCA 520(g); 21 USC 360j(g)]	Would not change current law.	Consistent with the purpose of this subsection, the Secretary would not be allowed to disapprove an IDE application because the Secretary determines that: (1) the investigation may not support a substantial equivalence or de novo classification determination or approval of a device; (2) the investigation may not meet a requirement, including a data requirement, relating to the approval or clearance of a device; or (3) an additional or different investigation may be necessary to support clearance or approval of the device. [Sec. 701]
Publication of information on 510(k) clearances requiring clinical data		
The Secretary is required under current law to publish specified information about safety and effectiveness of devices. [FFDCA 520(h); 21 USC 360j(h)]	Would not change current law.	Would require the Secretary to regularly publish detailed decision summaries for each 510(k) clearance that required clinical data; exceptions would apply for trade secrets. [Sec. 704]
Schedule to require promulgation of regulations for certain class III medical devices		
Under the Medical Device Amendments Act of 1976 (MDA), all pre-MDA devices were classified into one of three classes (class I, class II, class III); only class III required premarket review by FDA. All post-MDA devices were automatically placed in class III until reclassified. For a device type assigned to class III,	Would not change current law.	Would require the Secretary to establish, within 90 days of enactment, a schedule for the promulgation of regulations to require premarket approval (PMA) for each class III medical device that had been introduced into commerce before May 28, 1976, (or a device that is substantially

Current Law	S. 3187 (as passed)	H.R. 5651 (as passed)
MDA required FDA to promulgate a regulation calling for manufacturers of devices of that type to submit a PMA application. However, starting in the late 1970s, FDA regulated over 100 class III device types through the 510(k) program. This approach was intended to be temporary, and over time either FDA would reclassify such a device type into class I or class II or sustain the class III classification and call for PMA applications. [Note: The Safe Medical Devices Act of 1990 (P.L. 101-629) directed FDA to establish a schedule for promulgation of regulations calling for PMAs of devices that still used the 510(k) notification as an entry to the marketplace. Currently about 20 medical device types remain in this transitional state awaiting final classification.] [FFDCA 515; 21 USC 360e]		equivalent to such a device), for which no final regulation had been promulgated requiring premarket approval. Within one year after the schedule is established, the Secretary would have to issue a final regulation requiring premarket approval for each device the Secretary requires to remain in class III. [Sec. 711]
Harmonization of device premarket review, inspection, and labeling		
FFDCA Sec. 803 establishes an Office of International Relations and establishes related responsibilities for the Secretary. Specifically, the Secretary is required to support, as specified, methods and approaches to reduce the burden of regulation and harmonize regulatory requirements. FFDCA Sec. 803(c)(4) directed the Secretary to, within 180 days after enactment of FDAMA of 1997, make public a plan that establishes a framework for achieving mutual recognition of good manufacturing practices inspections. [FFDCA 803; 21 USC 383]	Would not change current law.	Would allow the Secretary, with respect to devices, to enter into arrangements with nations regarding approaches to harmonizing regulatory requirements for activities including inspections and common international labeling symbols. Within 3 years of enactment, the Secretary would submit to the House Committee on Energy and Commerce and the Senate Committee on Health, Education, Labor, and Pensions a report on FDA's harmonization activities. [Sec. 731]
Participation in international fora		
FFDCA Sec. 803(c) requires the Secretary to regularly participate in meetings with foreign governments to discuss and reach agreement on methods and approaches to harmonizing regulatory requirements. [FFDCA 803(c); 21 USC 383]	Would not change current law.	Would allow the Secretary to participate in fora, including the International Medical Device Regulators Forum and to (1) provide guidance on strategies, policies and other activities of a forum; (2) solicit review and consider comments from industry, academia, health care professionals, and patient groups regarding the fora activities; and (3) inform the public of fora activities. [Sec. 732]

Source: CRS analysis of current law, S. 3187 (as passed), and H.R. 5651 (as passed).

Human Drug Regulation

A key FDA responsibility is to regulate the safety and effectiveness of drugs sold in the United States. FDA divides that responsibility into two phases: *preapproval* (premarket) and *postapproval* (postmarket). FDA reviews manufacturers' applications to market drugs in the United States; a drug may not be sold unless it has FDA approval. The agency continues its oversight of drug safety and effectiveness as long as the drug is on the market. For an overview of FDA's responsibility in many of these areas, see CRS Report R41983, *How FDA Approves Drugs and Regulates Their Safety and Effectiveness*, by Susan Thaul.

Beginning with the Food and Drugs Act of 1906, Congress has incrementally refined and expanded FDA's responsibilities regarding drug approval and regulation. Members of the 112th Congress have suggested that FDA take additional efforts across the lifespan of its drug products. Provisions that either the Senate or House have passed cluster around encouraging product development, expediting application and review processes, attending to product integrity, preventing and mitigating drug shortages, and regulating medical gases. This report continues with each of those clusters, in the order they appear in the Senate bill. The drug regulation section ends with a cluster of individual provisions that, although labeled miscellaneous, each target an area of congressional concern and potential FDA responsibility.

Pharmaceutical Supply Chain[19]

FDA's earliest authorities, in 1906, concerned product integrity: Did the label accurately indicate the powdered and liquid ingredients in a bottle of elixir? Changes in the law reflected the mid-century pharmaceutical industry with mostly domestic factories. As drug production has shifted to a global chain of manufacturers, processers, packagers, importers, and distributors, FDA leadership, among others, has suggested that the agency's statutory tools do not match its responsibilities.[20] The agency, manufacturers, wholesalers, pharmacists, and consumers have suggested solutions to Congress. Some of those are formed as provisions in the Senate- and House-passed bills, as described in **Table 7**. Members continue discussions about chain-of-custody documentation, track-and-trace technologies and requirements, and anti-counterfeiting technology and enforcement tools, attempting to find an effective and feasible mix that covers domestic and foreign facilities.

[19] Susan Thaul, Specialist in Drug Safety and Effectiveness; Sarah A. Lister, Specialist in Public Health and Epidemiology; Vanessa K. Burrows, Legislative Attorney; and Erin Bagalman, Analyst in Health Policy, prepared this section of the report, with assistance from Judith M. Glassgold, Specialist in Health Policy. For follow-up discussions, contact Susan Thaul.

[20] Statement of Janet Woodcock, M.D., Director, FDA Center for Drug Evaluation and Research, before the Subcommittee on Oversight and Investigations, House Committee on Energy and Commerce, "FDA's Ongoing Heparin Investigation," April 29, 2008, http://www.fda.gov/NewsEvents/Testimony/ucm115242.htm.

Table 7. Pharmaceutical Supply Chain

Current Law	S. 3187 (as passed)	H.R. 5651 (as passed)
Registration of domestic drug establishments		
Every person who owns or operates any establishment in any state engaged in the manufacture, preparation, propagation, compounding, or processing of a drug or drugs must register with the Secretary each year. Required information is name, places of business, and all such establishments. [FFDCA 510(b,c); 21 USC 360(b,c)]	Would expand the registration information required to include each facility's unique facility identifier (which the section authorizes the Secretary to specify) and point-of-contact e-mail address. It also would change the timing of annual registration. Would also expand the requirements to include specified information about each drug importer that takes physical possession of and supplies to the person a drug (other than an excipient). Would require this information for every person immediately upon first engaging in the manufacture of a drug or device. [Sec. 701]	Would expand the registration requirements for an owner or operator of a domestic drug establishment to include a unique facility identifier. Would also change the timing of annual registration. [Secs. 808(a), 801(a)] [See also Sec. 810, below, regarding the registration of commercial importers.]
Registration of foreign establishments		
A product is deemed to be misbranded if it was manufactured, prepared, propagated, compounded, or processed in a domestic establishment not duly registered with the Secretary. [FFDCA 502(o); 21 USC 352(o)] A foreign establishment that manufacturers a drug or device that is imported or offered for import in the United States must register with specified information to the Secretary upon first engaging in the activity and then annually. [FFDCA 510(i); 21 USC 360(i)]	Would add foreign facilities to the misbranding section. [Sec. 702(a)] Would specify that the owner or operator of the foreign establishment would be responsible for the registration. Would expand the registration information required to include each facility's unique facility identifier (which the section authorizes the Secretary to specify) and point-of-contact e-mail address. It also would change the timing of annual registration. Would expand the information required concerning each drug importer and the importer's establishments. For foreign device establishments, this section would require specified registration information about known importers. It also would change the timing of annual registration. [Sec. 702(b)]	Would expand the registration requirements for an owner or operator of a foreign drug establishment to include a unique facility identifier. Would also change the timing of annual registration. [Secs. 808(b), 801(a)]
Registration of drug excipient information with product listing		
A registrant must file a list of drugs and devices with the Secretary according to specified criteria. [FFDCA 510(j); 21 USC 360(j)]	Would require, for any drug or device listed, the registrant to also provide information on each drug excipient establishment to include a unique facility identifier and point-of-contact e-mail address. [Sec. 703]	Would not change current law.

Current Law	S. 3187 (as passed)	H.R. 5651 (as passed)
Electronic system for registration and listing		
Registrations and listings must be submitted electronically unless the Secretary waives the requirement. [FFDCA 510(p); 21 USC 360(p)]	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. [Sec. 704]	Would not change current law.
Guidance on a unique facility identifier system		
No strictly comparable provisions. Owners and operators of certain manufacturing facilities are required to register with the Secretary. [FFDCA 510; 21 USC 360]	No provision regarding unique facility identifier guidance. [As summarized above, the Secretary's authority to assign unique facility identifier's would be created in Sec. 701 of the Senate bill.]	Would require the Secretary to provide guidance on a unique facility identifier system for domestic and foreign facilities and commercial importers to meet requirements of FFDCA Sec. 510(b)(1), (c), and (i)(1)(A), and FFDCA Sec. 801(s), as added by this title. [Sec. 808]
Risk-based inspection frequency		
All registered domestic establishments are subject to inspection. Those engaged in the manufacture of a drug or class II or class III device must be inspected at least once every 2 years. [FFDCA 510(h); 21 USC 360(h)]	Would require the Secretary to carry out inspection requirements according to a risk-based schedule to allocate inspection resources based on specified safety risks of establishments; to not distinguish between prescription and nonprescription products; and to submit publicly available annual reports to Congress. Would not change biennial requirement for class II and class III devices. [Sec. 705]	Similar to Senate provision. [Sec. 802]
Records for inspection		
Inspectors are authorized, upon written notice to the owner or operator, to enter a facility at reasonable times to inspect the facility and records. [FFDCA 704(a); 21 USC 374(a)]	Would require a manufacturer to electronically submit records required for inspection in a timely and reasonable manner at the manufacturer's expense; would require the Secretary to clearly describe records requested and to provide a confirmation receipt. [Sec. 706]	Similar to Senate provision; but would allow records to be submitted in physical or electronic form. [Sec. 815]
Failure to allow foreign inspection		
The Secretary of the Treasury [now, the Secretary of Homeland Security] has responsibilities regarding products imported or offered for import into the United States. [FFDCA 801(a); 21 USC 381(a)]	Would require the Secretary of Homeland Security, upon request from the HHS Secretary, to refuse to admit into the United States a product manufactured in an establishment that has refused to permit HHS inspection. [Sec. 707]	Would add requirement for importation of drugs that all commercial importers and foreign establishments provide unique facility identifier or article will be refused admission. [Sec. 808(d)] Would require the Secretary of Homeland Security to refuse to admit a drug offered for import into

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		the United States that did not have all documentation that the HHS Secretary may require, including certification of inspections. [Sec. 809]
Protection of confidential inspection information obtained from a foreign government		
The Freedom of Information Act (FOIA) requires federal agencies to disclose information about the work they conduct, upon request. FOIA exempts certain types of information from disclosure, including sensitive national security information, and trade secrets and commercial or financial information obtained from a person that is privileged or confidential.[a] [5 USC 552] FDA routinely receives the trade secret information from medical product sponsors in the course of product review, investigations, and related activities. FDA may disclose information otherwise protected under FOIA to its contractors, as long as FDA assures that the contractor can protect such information from further disclosure. [FFDCA 708; 21 USC 379] The Secretary may declare the existence of a public health emergency, and take certain actions.[b] [PHSA 319; 42 USC 247d]	Would amend FFDCA Sec. 708 with a new paragraph (b) to prohibit the Secretary from disclosing, under the Freedom of Information Act or other laws, information relating to drug inspections obtained from a foreign government if the Secretary determines that the following conditions have been met: the information was provided voluntarily to the U.S. Government and on the condition that the information not be publicly released; and the foreign government agency makes a written request that the information be kept confidential. Foreign governments would be able to specify in their requests that the voluntarily-provided information be withheld from disclosure for a particular time period, but if no time period is specified, then the withholding period is up to three years. Would amend FFDCA Sec. 708 with a new paragraph (c) to authorize the Secretary, In specified circumstances, to share certain drug-related trade secret information through written agreement with foreign governments that the Secretary has certified as able to protect trade secret information from disclosure. Such foreign government would be required to commit in writing to protect such information unless the sponsor gave written permission for disclosure, or the Secretary made a declaration of a public health emergency under section 319 of the PHSA that is relevant to the information. The Secretary could disclose information about facility inspections to such foreign government if such government has authority to otherwise obtain such information, and uses it for civil regulatory purposes. The Secretary could disclose other types of information as part of an investigation if the Secretary "has reasonable grounds to believe that a	Would amend FFDCA Sec. 708 with a new paragraph (b) to exempt drug-related information obtained by the Secretary from disclosure under FOIA and other laws, when such information is provided by a federal, state, local, or foreign government agency that has requested that the information be kept confidential (except pursuant to court order). The House bill includes language that is substantively identical to the Senate provision for a new FFDCA Sec. 708(c), except that it *does not explicitly mention "humans and animals"* in the final phrase describing reasonable grounds for other disclosures. [Sec. 812]

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	drug has a reasonable probability of causing serious adverse health consequences or death *to humans or animals*." [Sec. 708]	
Current good manufacturing practices (CGMPs)		
Under the FFDCA, a drug is deemed adulterated if, among other things, its manufacture, processing, packing, or holding does not conform to current good manufacturing practices, to assure that it meets FFDCA requirements for safety, identity, strength, quality, and purity. [FFDCA 501(a)(2)(B); 21 USC 351(a)(2)(B)]	Would amend FFDCA Sec. 501 to clarify, with respect to criteria for deeming a drug to be adulterated, that "current good manufacturing practices" include quality controls in manufacturing, and assurance of raw material safety. [Sec. 709]	The House bill includes a provision that is substantively identical, although it would amend FFDCA Sec. 501 in a different place. [Sec. 803]
Third-party accreditation: program in general		
No provision regarding drugs. However, the FFDCA requires the Secretary to establish a third-party accreditation system for inspection of imported foods. That system has three required elements in law, namely: (1) processes whereby the Secretary recognizes accrediting bodies to accredit third-party auditors; (2) processes whereby such accrediting bodies accredit third-party auditors; and (3) processes whereby accredited third-party auditors conduct food safety audits (i.e., inspections) in order to assure compliance with FFDCA requirements. [FFDCA 808; 21 USC 384d] The FFDCA authorizes a related program for medical devices, in which the Secretary directly accredits third parties to conduct reviews and inspections. [FFDCA 523(c); 21 USC 360m(c), and FFDCA 704(g)(11); 21 USC 374(g)(11)]	Would establish a new FFDCA Sec. 809 requiring the Secretary, within 2 years of enactment, to establish an accreditation system for third-party audits to assure drug safety. The system would contain the same general elements as the food safety accreditation program under current law. Would establish procedures to mitigate conflicts of interest among accrediting bodies and third-party auditors. False statements made by employees or agents of an accrediting body or third-party auditor would subject those persons to fines and/or imprisonment. A GAO report addressing specified aspects of the program would be required by January 20, 2017. [Sec. 710]	No provision.
Third-party accreditation: requirements of the Secretary		
No provision.	The Secretary would be required to, among other things: (1) develop model standards, with specified elements, for the accreditation of third-party auditors within 18 months of enactment; (2) use audit results to inform the drug risk-based inspection schedule; (3) revoke recognition of an accrediting body for failure to comply with requirements, through a specified	No provision.

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	process (which includes a reinstatement process); (4) revoke accreditation of a third- party auditor that fails to comply with requirements, or refuses to allow federal officials to conduct an investigation to assure compliance, after opportunity for informal hearing (re-accreditation procedures also are provided); (5) publish on the FDA website a list of recognized accrediting bodies and accredited third-party auditors; (6) monitor program performance through periodic review of the performance of accrediting bodies and third-party auditors, including by conducting audits; (7) use audit results to establish the risk-based inspection schedule for drugs, as would be established under Sec. 705 of this bill; and (8) finalize implementing regulations, according to specified procedures, within 18 months of enactment. [Sec. 710]	
Third-party accreditation: authorities of the Secretary		
No provision.	The Secretary would be authorized to, among other things: (1) directly accredit third-party auditors, including foreign governments, under certain conditions; (2) revoke accreditation of a third-party auditor if recognition of its accrediting body has been revoked. [Sec. 710]	No provision.
Third-party accreditation: requirements of accrediting bodies		
No provision.	Recognized accrediting bodies would be required to, among other things: (1) submit to the Secretary a listing of all accredited third-party auditors, to include specified information; and (2) before accrediting a foreign government or any other third-party auditor, review and audit drug safety programs, processes, systems, and standards, to assure that drugs certified by such government or other third party would meet FFDCA requirements. [Sec. 710]	No provision.
Third-party accreditation: requirements of third-party auditors		
No provision.	Accredited third-party auditors would be required to, among other things: (1) provide audit findings to FDA upon request; (2) agree to provide written documentation to the Secretary regarding an	No provision.

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	establishment's compliance with FFDCA Sec. 501 (which deems a drug adulterated unless numerous conditions, generally involving CGMPs, are met); and (3) report to the Secretary any conditions that pose a serious risk to public health. They could also conduct audits upon the voluntary request of an establishment (called "consultative audits"), in which findings would in general not be available to the Secretary. [Sec. 710]	
Third-party accreditation: fees		
No provision.	Would authorize the Secretary to collect fees from recognized accrediting bodies and accredited third-party auditors, only in such amounts necessary to administer the accreditation program. Fees would be authorized only to the extent and in the amount provided in advance in appropriation acts, and would remain available until expended. A recognized accrediting body could assess a reasonable fee to accredit third-party auditors. [Sec. 710]	No provision.
Standards for admission of imported drugs		
The Secretary may refuse admission to drugs or medical devices presented for import if the importer, owner, or consignee of such product does not provide the Secretary with information identifying the registered establishment or establishments, as required under FFDCA Sec. 510(i). [FFDCA 801(o); 21 USC 381(o)]	Would amend FFDCA Sec. 801(o) to remove its application to drugs. 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 would be required to finalize regulations in a specified manner within 18 months of enactment, taking into consideration the type of import, such as whether the drug is for import for use in preclinical or clinical investigation. [Sec. 711]	The House bill includes a provision similar to that in the Senate bill. It would allow the Secretary to require documentation or other information by a drug importer as a condition of granting entry, although the bill does not state that such information must be in electronic form. The Secretary would be required to specify the required documentation or other information (which could include such information as stated in the Senate bill) through rulemaking. Such requirements would be effective not less than 180 days after a final rule was promulgated. The Secretary could exempt drugs imported solely for research purposes, and other types of drug imports, from some or all of the requirements. [Sec. 809]
Notification requirement for harmful, stolen, or counterfeit drugs		
No provision. However, the House and Senate bills refer to persons required to register under FFDCA Sec. 510, which requires persons to register establishments engaged in manufacture, preparation,	Would create a new FFDCA Sec. 568, which would allow the Secretary to require notification by *two* types of "*covered persons*" if they know (1) of a substantial loss or theft of the drug, or (2) the drug has	Would allow the Secretary to require similar, but not identical, notification by *three* types of "*regulated persons*" if they know (1) *that the use of such drug in the United States may result in serious injury or*

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propagation, compounding, or processing of a drug.	been or is being counterfeited and the counterfeit product is either in U.S. commerce *or is being offered for import into the United States.*	*death,* (2) of a substantial loss or theft of the drug *intended for use in the United States,* or (3) that the drug has been or is being counterfeited and the counterfeit product is either in U.S. commerce *or has been or is being imported into the United States or may reasonably be expected to be offered for import into the United States.*
	Defines "*covered persons*" as: (1) persons required to register establishments under FFDCA Sec. 510, as well as (2) persons engaged in wholesale distribution, *as defined in FFDCA Sec. 503(e)(3)(B).*	Defines "*regulated persons*" as: (1) persons required to register under FFDCA Sec. 510 *or under a new FFDCA provision for the registration of commercial importers under Sec. 801(s) (as would be established by this bill),* (2) a wholesale distributor of a drug product *(unlike S. 3187, not specifically defined)*, or (3) *any other person that distributes drugs except a person that distributes drugs exclusively for retail sale.*
	Would require notification to be *made in a reasonable time, in such reasonable manner, and by such reasonable means* as the Secretary may require in regulation (which would have the force of law) or specify in guidance (which would not be legally binding). *Would clarify that the requirement could be imposed for losses, theft, or counterfeiting that occurred on or after enactment.* [Sec. 712(b)]	Would also require notification *made in such manner and by such means* as the Secretary may specify by regulation or guidance, but *would not include the Senate language regarding reasonable time, manner, and means.* *Does not contain the clarification in the Senate bill regarding losses, theft, or counterfeiting that occurred after enactment.* [Sec. 811(b)] *Unlike the Senate bill, contains a savings clause that states this provision shall not be construed as limiting the Secretary's authority to require notifications related to a drug under the FFDCA or PHSA.*
FFDCA Sec. 301 lists a number of "prohibited acts," generally violations of requirements elsewhere in the Act. If a person is convicted of violating a prohibited act, pursuant to FFDCA Sec. 303, that person (which could be a corporation) may be subject to civil or criminal penalties. [FFDCA 301; 21 USC 331, and FFDCA 303; 21 USC 333]	Would add a new prohibited act to FFDCA Sec. 301, based on the failure to notify the Secretary, as specified in the new FFDCA Sec. 568 *as proposed in the Senate bill.* [Sec. 712(a)]	Would also add a new prohibited act to FFDCA Sec. 301, based on the failure to notify the Secretary, as specified in the new FFDCA Sec. 568 *as proposed in the House bill.* [Sec. 811(a)]
Protection against intentional adulteration		
Current law does not explicitly address the intentional adulteration of drugs. As noted above, FFDCA Sec. 303 provides for civil and/or criminal penalties for violations of the FFDCA. FFDCA subsections	Would provide that any person that knowingly and intentionally adulterates a drug such that it is adulterated under FFDCA 501(a)(1), (b), (c), or (d) and has a reasonable probability of causing serious	The House bill contains an identical provision. [Sec. 814]

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501(a)(1), (b), (c) and (d) refer to drugs deemed adulterated because: they are filthy, putrid, or decomposed; they are impure; or they have lost potency.	adverse health consequences or death to humans or animals shall be imprisoned for not more than 20 years, or fined not more than $1 million, or both. [Sec. 713]	
Enhanced criminal penalty for counterfeiting drugs		
FFDCA Sec. 301(i) prohibits forging, counterfeiting, and misrepresentation. As noted above, FFDCA Sec. 303 provides for civil and/or criminal penalties for acts prohibited under FFDCA Sec. 301. Sec. 303 provides for fines and/or imprisonment for violations of Sec. 301 in general, and also stipulates a number of specific actions that are subject to enhanced fines or longer terms of imprisonment. Sec. 303 does not currently provide for enhanced criminal penalties for counterfeiting. [FFDCA 301(i); 21 USC 331(i), and FFDCA 303; 21 USC 333]	Would amend FFDCA Sec. 303(b) to provide that any person who knowingly and intentionally violates FFDCA Sec. 301(i) would be imprisoned for not more than 20 years, or fined not more than $4 million, or both. *This provision does not appear to be limited to counterfeiting of drugs.* [Sec. 714]	Also would amend FFDCA Sec. 303(a) to provide e*nhanced penalties explicitly for counterfeiting of drugs in violation of FFDCA Sec. 301(i).* [Sec. 807]
Title 18 of the U.S. Code is the criminal and penal code, under which fines and/or imprisonment may be imposed for violations of federal law. 18 USC 2320 prohibits trafficking in counterfeit goods or services (not specific to drugs), and provides for the following penalties for knowing and reckless violations: • *For a first offense, a fine of not more than $2 million and/or imprisonment of up to 10 years for an individual, or a fine of not more than $5 million for a person other than an individual.* • *For each offense after the first, a fine of not more than $5 million and/or imprisonment of up to 20 years for an individual, or a fine of not more than $15 million for a person other than an individual.* • *For an offense that causes serious bodily injury, a fine of not more than $5 million and/or imprisonment of up to 20 years for an individual, or a fine of not more than $15 million for a person other than an individual.* • *For an offense that causes death, a fine of not more than $5 million and/or imprisonment of up any*	Would amend 18 USC 2320 to impose the following increased penalties for a person who knowingly traffics in counterfeit drugs: • *For a first offense, a fine of not more than $4 million and/or imprisonment of up to 20 years for an individual, or a fine of not more than $10 million for a person other than an individual.* • *For each offense after the first, a fine of not more than $8 million and/or imprisonment of up to 20 years for an individual, or a fine of not more than $20 million for a person other than an individual.* [Sec. 714]	Would impose the following increased penalties for a person who knowingly traffics in counterfeit drugs, *which differ somewhat from the Senate provision:* • *Imprisonment of not more than 20 years (with or without the applicable fine); and* • *If use of the counterfeit drug is the proximate cause of the consumer's death, the term of imprisonment shall be any term of years or for life.* [Sec. 807]

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term of years or for life for an individual, or a fine of not more than $15 million for a person other than an individual.		
The Sentencing Reform Act of 1984 (Chapter II of the Comprehensive Crime Control Act of 1984, P.L. 98-473) created the United States Sentencing Commission, an independent body within the federal judicial branch charged with promulgating guidelines for federal sentencing. [28 USC 991]	Would require the U.S. Sentencing Commission to review its guidelines and policies, as specified, in order to take into consideration the intent of Congress that penalties for persons convicted of a drug counterfeiting offense under 18 USC 2320 should be increased in comparison to current guidelines and policies. [Sec. 714]	No provision.
Extraterritorial jurisdiction		
The FFDCA does not contain references to extra-territoriality, the application of American criminal laws outside of the United States.[c]	Would make extraterritorial violations of the FFDCA subject to enforcement in the United States if either (1) the article was intended for import into the United States or (2) an act in furtherance of the violation was committed in the United States. In the absence of this express grant, the statute's provisions would most likely have only territorial application.[d] [Sec. 715]	The House bill contains an identical provision. [Sec. 813]
Compliance with international agreements		
The United States has obligations under international agreements that, inter alia, prohibit the adoption of certain measures banning, regulating, or according less favorable treatment to imports.	Would require courts and administrative agencies to interpret and apply the FFDCA consistent with international agreements to which the United States is a party.[e] [Sec. 716]	No provision.
Prohibitions against delaying, denying, limiting, or refusing inspection		
FFDCA Sec. 501 lists several situations under which a drug or device must be deemed adulterated. Adulteration of a drug is a prohibited act under the FFDCA, and a person convicted of a prohibited act faces criminal penalties authorized by the FFDCA, discussed above. [FFDCA 501; 21 USC 351]	Would not change current law.	Would add a new provision to the list in FFDCA Sec. 501. If a drug has been manufactured, processed, packed, or held in any factory, warehouse, or establishment and the owner, operator, or agent of such factory, warehouse, or establishment delays, denies, or limits an inspection, or refuses to permit entry or inspection, then the drug must be deemed to be adulterated. Also would require the Secretary to issue, within 1 year of enactment, guidance that defines the circumstances that would constitute delaying, denying, or limiting inspection for the purposes of the new FFDCA provision.[f] [Sec. 804]

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Destruction of adulterated, misbranded, or counterfeit drugs offered for import		
FFDCA Sec. 801(a) provides that an article must be refused admission into the United States, with some exceptions, on the following bases: "If it appears from the examination of [samples of drugs which are being imported or offered for import into the United States] or otherwise that (1) such article has been manufactured, processed, or packed under unsanitary conditions…, or (2) such article is forbidden or restricted in sale in the country in which it was produced or from which it was exported, or (3) such article is adulterated, misbranded, or in violation of FFDCA Sec. 505 [re: new drugs], or prohibited from introduction or delivery for introduction into interstate commerce under FFDCA Sec. 301(ll) [certain food to which drugs or biological products have been added] .... " The FDA's authority to detain without physically inspecting an article derives from the words "or otherwise" in FFDCA Sec. 801(a). FDA decisions to refuse an import are final agency actions reviewable for abuse of discretion. Under Sec. 801(a), an article refused admission must be destroyed if it is not exported within 90 days of the date of the notice of the refusal, or within an additional allotment of time prescribed by regulation. Statutes, regulations, and memoranda of understanding that refer to functions performed by the Secretary of the Treasury are now undertaken by the Secretary of the Department of Homeland Security (U.S. Customs and Border Protection (CBP)) pursuant to Sec. 403(1) of P.L. 107-296 (the Homeland Security Act of 2002), 19 C.F.R. Secs. 0.1-0.2.	Would not change current law.	Would amend FFDCA Sec. 801(a) allowing the HHS Secretary, in consultation with the Secretary of Homeland Security, to destroy, without the opportunity for export, any drug refused admission that (1) has reasonable probability of causing serious adverse health consequences or death, as determined by the HHS Secretary, or (2) is valued at $2,000 or less. Would enable the Secretary of Homeland Security to increase the dollar value through regulation. Would require the HHS Secretary to issue regulations providing notice and an opportunity for a hearing on the destruction of the drug under this new provision. Notice and the opportunity for a hearing for the owner or consignee could occur before or after the drug is destroyed, unless the drug was worth more than $2,000 (or the value adjusted by regulation) and the HHS Secretary has determined the drug has a reasonable probability of causing serious adverse health consequences or death. In that case, the regulations would have to provide notice and an opportunity for a hearing before the destruction occurs. Would require the HHS Secretary's regulations to establish an administrative process through which an owner or consignee of a drug destroyed without opportunity for a hearing could obtain restitution for the value of the destroyed drug if the drug was wrongfully destroyed. Would eliminate the requirement in FFDCA Sec. 801(a) that the Secretary of Homeland Security give notice to the owner or consignee before delivering samples, upon request, to the HHS Secretary, of drugs being imported or offered for import. [Sec. 805]
Administrative detention		
FFDCA Sec. 304(g) provides for administrative detention of devices and tobacco pursuant to an inspection of a facility or vehicle. FFDCA Sec. 304(h) treats the	Would not change current law.	Would amend FFDCA Sec. 304(g) so that it applies to drugs as well. This amendment would not take effect until the Secretary issues a final implementing regulation. The

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administrative detention of food differently from devices and tobacco. If, during an inspection under FFDCA Sec. 704, the officer or employee making the inspection has reason to believe that the device or tobacco product is adulterated or misbranded, that individual may order the device or tobacco product detained, in accordance with regulations, for up to 20 days. If the Secretary determines that a greater time period is required in order to institute a court action to seize and condemn the device or tobacco product or for an injunction or restraining order, the Secretary may authorize a detention of up to 30 days. Regulations must provide that before a device or tobacco product may be ordered detained, that the Secretary or a designated officer or employee must approve the order. Detention orders may require labeling or marking during the detention for purposes of identifying the device or tobacco product as detained. Persons entitled to claim the detained device or tobacco product if it had been seized may appeal the detention to the Secretary, and the Secretary must provide an opportunity for an informal hearing to confirm or revoke the detention within 5 days of when the appeal is filed. Devices and tobacco products under a detention order must not be moved from the place of detention unless released by the Secretary or the expiration of the detention period, whichever occurs first. However, a device under a detention order may be moved in accordance with regulations if it is not in final form for shipment, at the manufacturer's discretion for the purpose of completing the work required to put the device into final form for shipment. [FFDCA 304(g); 21 USC 334]		Secretary would be required to issue such a regulation within 2 years of enactment. Before issuing such a regulation, the Secretary would be required to consult with stakeholders, including drug manufacturers. [Sec. 806]
Registration of commercial importers		
Owners and operators of certain manufacturing facilities are required to register with the Secretary. [FFDCA 510; 21 USC 360] FFDCA requires certain actions	Would not change current law.	Would prohibit importation of drugs by unregistered commercial importers. Would amend FFDCA Sec. 801 to require registration of commercial

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regarding imported FDA-regulated products. [FFDCA 801; 21 USC 381] FFDCA lists prohibited acts and situations in which a product would be deemed misbranded. [FFDCA 301; 21 USC 331, and FFDCA 502(o); 21 USC 352(o)]		importers with the Secretary; such registration would include the submission of a unique identifier for the principal place of business of the importer. Would require the Secretary, in consultation with the Secretary of Homeland Security, to, by regulation, establish good importer practices to ensure drugs are in compliance with the FFDCA and PHSA. Would authorize the Secretary to, as appropriate, establish exemptions to this requirement and an expedited clearance process for certain importers based on the level of risk posed by the imported drug. Would require the Secretary to discontinue the registration of any commercial importer that fails to comply with these regulations. Would deem misbranded any drug that was imported or offered for import by a non-duly registered commercial importer. The Secretary, in consultation with the Secretary of Homeland Security, will be required to establish an effective date and promulgate regulations not later than 36 months after enactment. [Sec. 810]
RxTEC system		
Provisions throughout the FFDCA address aspects of pharmaceutical supply chain security. There is no consolidated section in current law such as the proposed RxTEC provisions.	Would add a new FFDCA Subchapter H (Pharmaceutical Distribution Integrity), beginning with a new FFDCA Sec. 581, which would define: data carrier, individual saleable unit, product, product tracing, RxTEC, suspect product, and verification. Would add new FFDCA Sec. 582 to establish an RxTEC systems to ensure the safety of the pharmaceutical distribution supply chain. RxTEC is defined as: "a data carrier that includes the standardized numerical identifier (SNI), the lot number, and the expiration date of a product. The standard data carrier RxTEC shall be a 2D data matrix barcode affixed to each individual saleable unit of a product and a linear or 2D data matrix barcode on a homogenous case of a product. Such information shall be both	No provision.

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	machine readable and human readable." Would create *manufacturer* requirements (to take effect not later than 4-1/2 years after enactment), *repackager* requirements (to take effect not later than 5-1/2 years after enactment), *wholesale distributor* requirements (to take effect not later than 6-1/2 years after enactment), and *dispenser* requirements (to take effect not later than 7-1/2 years after enactment) relating to specified *product tracing*, *verification*, and *notification of product removal* activities. Would specify how requirements of the new FFDCA Sec. 582 should be applied to ensure flexibility. Would authorize the Secretary to issue guidance and would specify the process to be used if the Secretary promulgates any regulation pursuant to this section. Would require the Secretary, in consultation with appropriate federal officials and specified categories of stakeholders, to "prioritize and develop standards for the interoperable exchange of ownership and transaction information for tracking and tracing prescription drugs." [Sec. 722(a)] Would further amend FFDCA Sec. 301 (as amended by Sec. 712) by adding a violation of the new FFDCA Sec. 582 as a prohibited act. [Sec. 722(b)] Would require the Secretary, within 180 days of enactment, to issue a compliance guide to assist small entities in complying with the new FFDCA Sec. 582. [Sec. 722(c)]	
RxTEC system: effective date and preemption		
No provision. California Business and Professions Code, section 4034.1, states: (a) (1) Upon the effective date of federal legislation or adoption of a federal regulation addressing pedigree or serialization measures for dangerous drugs, Sections 4034, 4163, 4163.1, 4163.2, 4163.4, and 4163.5 shall become inoperative. (2)	Would preserve relevant state and local laws and regulations, including a California law that specifically addresses preemption by federal law or regulations. This provision would make subsection (c) and the amendments made by subsections (a) and (b) effective on either January 1, 2022, or once Congress enacts an express preemption provision for state law regulating the distribution	No provision.

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Within 90 days of the enactment of federal legislation or adoption of a regulation addressing pedigree or serialization measures for dangerous drugs, the board shall publish a notice that Sections 4034, 4163, 4163.1, 4163.2, 4163.4, and 4163.5 are inoperative. (3) Within 90 days of the enactment of federal legislation or adoption of a regulation that is inconsistent with any provision of California law governing the application of any pedigree or serialization requirement or standard, the board shall adopt emergency regulations necessary to reflect the inoperation of state law. (b) (1) If the Food and Drug Administration (FDA) enacts any rule, standard, or takes any other action that is inconsistent with any provision of California law governing application of a pedigree to a dangerous drug, that provision of California law shall be inoperative. (2) Within 90 days of the FDA enacting any rule, standard, or taking any other action that is inconsistent with any provision of California law governing application of a pedigree to a dangerous drug, the board shall publish a notice that the provision is inoperative. (3) Within 90 days of the FDA enacting any rule, standard, or taking any other action that is inconsistent with any provision of California law governing application of a pedigree to a dangerous drug, the board shall adopt emergency regulations necessary to reflect the inoperation of state law. (c) If the board fails to recognize the inoperation within 90 days pursuant to this section, nothing in this section shall preclude a party from filing an action in state or federal court for declaratory or injunctive relief as an alternative to filing a petition with the board.	of drugs, whichever is later. Would provide that nothing in this subtitle shall preempt any state or local law or regulation. Additionally, notwithstanding any other provision of federal or state law, including any amendments that would be made by subsection (a), the subsection must not trigger the preemption provisions in California Business and Professions Code, section 4034.1, which would invalidate various provisions of California's law once relevant federal legislation or regulations become effective, or once the FDA takes certain actions that are inconsistent with California's law on the application of pedigrees to dangerous drugs. The effective date of subsection (c), and the amendments to existing law made by subsections (a) and (b) would take effect on January 1, 2022, or on the date which Congress enacts a law providing for express preemption of any state law regulating the distribution of drugs, whichever is later. [Sec. 722(d)]	
Independent assessment of drug approval processes		
No provision.	Would require the Secretary to contract with a private, independent consulting firm to conduct a comprehensive assessment of the process for the premarket review of drug applications. The two-phase	No provision.

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	assessment would include participation of FDA and manufacturers, specified content, and a requirement that the Secretary analyze recommendations and develop and implement a corrective action plan. [Sec. 723]	

Source: CRS analysis of current law, S. 3187 (as passed), and H.R. 5651 (as passed).

Notes: Italics are provided to emphasize differences between bills.

a. CRS Report R41933, *Freedom of Information Act (FOIA): Background and Policy Options for the 112th Congress*, by Wendy Ginsberg.

b. See CRS Report RL33579, *The Public Health and Medical Response to Disasters: Federal Authority and Funding*, by Sarah A. Lister.

c. For information on the concept of extraterritoriality, see CRS Report 94-166, *Extraterritorial Application of American Criminal Law*, by Charles Doyle, and CRS Report 97-589, *Statutory Interpretation: General Principles and Recent Trends*, by Larry M. Eig.

d. See Morrison v. National Australia Bank Ltd., 130 S. Ct. 2869, 2877-78 (2010); EEOC v. Arabian American Oil Co., 499 U.S. 244, 248 (1991); Foley Brothers v. Filardo, 336 U.S. 281, 284-85 (1949); United States v. Yousef, 327 F.3d 56, 86 (2d. Cir. 2003).

e. In practice, this provision would likely require administrative agencies to adopt and maintain implementing regulations that comport with provisions of the World Trade Organization (WTO) Agreements on Technical Barriers to Trade (TBT Agreement), the WTO Agreement on Sanitary and Phytosanitary Measures (SPS Agreement), the General Agreement on Tariffs and Trade (GATT), and the related chapters of U.S. free trade agreements. Section 716 is not, however, limited to international trade agreements, and other binding international agreements may be implicated.

f. Although this provision would require the Secretary to issue guidance, guidance documents are not legally binding on courts or persons outside the agency. As an Office of Management and Budget (OMB) Bulletin has noted, "while a guidance document cannot legally bind, agencies can appropriately bind their employees to abide by agency policy as a matter of their supervisory powers over such employees without undertaking pre-adoption notice-and-comment rulemaking." 72 Fed. Reg. 3432, 3437 (Jan. 25, 2007).

g. The bill does not spell out RxTEC. The acronym refers to the Pharmaceutical Traceability Enhancement Code (RxTEC) developed by the Pharmaceutical Distribution Security Alliance (see, for example, Testimony of Shawn M. Brown, Vice President of State Affairs, Generic Pharmaceutical Association, before the Energy and Commerce Subcommittee on Health, U.S. House of Representatives, March 8, 2012, http://republicans.energycommerce.house.gov/Media/file/Hearings/Health/20120308/HHRG-112-IF14-WState-BrownS-20120308.pdf).

Incentives for Anti-Infective Drugs[21]

The treatment of infectious diseases often depends on the availability of anti-infective drugs. Approved drugs can become ineffective if infectious organisms develop resistance to them. However, development of new anti-infective drugs is not always attractive to sponsors; the drugs are often used short-term and/or in small numbers of patients, compared with so-called "blockbuster" drugs. In addition, some drug companies cite unique regulatory challenges in the approval of anti-infective drugs.

Types of Anti-Infective Drugs

An *antibiotic* or *antibacterial drug* treats a bacterial disease, such as a *Staph* infection.

An *antifungal drug* treats a fungal disease, such as *Candida* (a yeast infection).

An *antiviral drug* treats a viral disease, such as HIV.

An *antiparasitic drug* treats a parasitic disease, such as malaria.

The terms *anti-infective* and *antimicrobial* refer to any of the types of drugs above.

S. 3187 and H.R. 5651 propose to offer incentives for the development of certain new anti-infective drugs by providing an extended period of exclusivity, i.e., a period in which the new drug may be marketed without generic competition. The bills stipulate the types of new anti-infective drugs that would qualify for incentives. These provisions, summarized and compared in **Table 8**, are modified from the freestanding Generating Antibiotic Incentives Now Act of 2011 (GAIN Act), S. 1734/H.R. 2182.

Among other differences between the bills, the Senate bill limits eligible products to those that would be used to treat serious or life-threatening infections, while the House bill would offer such incentives to any type of anti-infective drug that would otherwise qualify. Members of Congress disagree on which approach would be more effective in spurring the development of new drugs to treat serious infections.[22]

[21] Sarah A. Lister, Specialist in Public Health and Epidemiology, prepared this section of the report.

[22] Alaina Busch and Nanci Bompey, "User Fees Clear E&C, But Waxman, Consumer Advocates Seek GAIN Changes," *FDA Week*, May 11, 2012.

Table 8. Incentives for Anti-Infective Drugs

Current Law	S. 3187 (as passed) Title VIII	H.R. 5651 as passed) Title VIII, Subtitle C
Definition of eligible product: qualified infectious disease product		
No provision.	Defines qualified infectious disease products (QIDPs) as *antibacterial or antifungal drugs intended to treat serious or life-threatening infections, including those caused by qualifying pathogens (QPs).* This would not include: supplemental applications for QIDPs that have or had an exclusivity period; or changes that result in a new indication, route of administration, dosing schedule, dosage form, delivery system, or delivery device. [Sec. 801]	Defines qualified infectious disease products (QIDPs) as *an antibacterial or antifungal drug for human use that treats or prevents an infection caused by a qualifying pathogen* (QP). This would not include: supplemental applications for QIDPs that have or had an exclusivity period; or changes that result in a new indication, route of administration, dosing schedule, dosage form, delivery system, delivery device, *or strength, or that do not result in a change in safety or effectiveness.* [Sec. 831] (See also Sec. 835, Guidance on Pathogen-Focused Antibacterial Drug Development, below.)
Definition of qualifying pathogen		
No provision	Defines a qualifying pathogen (QP) as "a pathogen identified and listed by the Secretary…that has the potential to pose a serious threat to public health." Stated *examples include* specific drug-resistant gram-positive and gram-negative bacteria (including tuberculosis), and Clostridium difficile. *QPs would be listed publicly, and such list revised by the Secretary through regulation every 5 years.* [Sec. 801]	Defines a qualifying pathogen (QP) *as one of a number of stated QPs that are* specific drug-resistant gram-positive and gram-negative bacteria (including tuberculosis), *or any other pathogen identified for this purpose by the Secretary*. [Sec. 831]
Certification by the Secretary		
No provision.	Would allow a sponsor to request designation of a drug that meets the criteria above as a QIDP *at any time prior to submission of the application*. Would require the Secretary to render a decision *within 60 days* of request. *The designation would be irrevocable unless the request contained an untrue statement of material fact.* [Sec. 801]	Would allow a sponsor to request designation of a drug that meets the criteria above as a QIDP *at any time that is at least 45 days prior to submission of the application*. Would require the Secretary to render a decision *within 30 days* of request. [Sec. 831]
Market exclusivity		
Current law does not, in general, treat anti-infective drugs differently from other drugs with regard to market exclusivity. Certain new chemical entities, new drug indications, and orphan drugs (including anti-infective drugs) may be eligible for terms of exclusivity ranging, in total,	QIDPs would be eligible for an additional 5 years of market exclusivity, in addition to any periods of exclusivity for which such drugs would otherwise qualify. [Sec. 801]	Would also provide QIDPs with an additional 5 years of exclusivity. [Sec. 831]

Current Law	S. 3187 (as passed) Title VIII	H.R. 5651 as passed) Title VIII, Subtitle C
from 3 to 7 years.[a] Certain pediatric drugs may be eligible for an additional 6 months of exclusivity.		
Regulations		
No provision.	Would require final regulations, following specified procedures, *within 2 years of enactment. The Secretary could designate drugs as QIDPs prior to promulgation of regulations.* [Sec. 801]	Would require final regulations *within 1 year of enactment.* [Sec. 831]
Approval process		
In general, priority review is not defined in law. However, in practice, FDA may prioritize review of certain types of applications among those it receives. Fast track review requires the Secretary to offer expediting procedures, such as pre-application meetings with sponsors, for a designated fast track product, defined as one intended to treat a serious or life-threatening condition, and that demonstrates the potential to address unmet medical needs for such a condition.[b] [FFDCA 506; 21 USC 356]	Would make QIDPs eligible for priority review (which is not defined) [Sec. 802] and fast track review (as amended by Sec. 901 of this bill) [Sec. 803]	No provision.
GAO report		
No provision.	Would require GAO to report, within 1 year of enactment, on the possible need for incentives *for biological products and antifungal drugs (with recommendations), as well as a number of specified regulatory matters, including an assessment of QIDP regulatory, review, and development issues.* [Sec. 804] (See also GAO report on guidance documents, below.)	Also would require GAO to report, within 1 year of enactment, on the possible need for incentives *for biological products (with recommendations). Does not explicitly require reporting on specific regulatory matters.* [Sec. 832]
Clinical trials guidance and recommendations		
No provision.	Would require the Secretary to review and, if needed, to update *no fewer than 3 guidance documents per year* regarding the conduct of clinical trials for antibacterial and antifungal drugs, and would require the Secretary to provide written recommendations for such trials, upon the request of a sponsor seeking approval of a QIDP. *Would require* a GAO study of clinical trial guidance documents. [Sec. 805]	Similar to Senate bill, would require review of guidance documents. However, such review would have to be completed *within 1 year of enactment, and repeated within 4 years of enactment.* Also would require the Secretary to make recommendations re: clinical trials upon sponsor's request. *Would not require* a GAO study of clinical trial guidance documents. [Sec. 833]

Current Law	S. 3187 (as passed) Title VIII	H.R. 5651 as passed) Title VIII, Subtitle C
Strategy and reassessment		
No provision.	*Would require* the Secretary to report to Congress, within 1 year of enactment, with a strategy and implementation plan regarding the requirements of this title. Also would require the Secretary, *within 3 years of enactment* to report to Congress on progress, including on the number and list of QIDPs, QIDP submissions, approvals, and review times. Would not require such report to include recommendations. [Sec. 806]	*Would not require* the Secretary to develop a strategy and implementation plan. Would require the Secretary, *within 5 years of enactment,* to report to Congress on implementation of the incentives program, including information mentioned in the Senate bill, *in addition to whether products approved under the program met the need to treat serious and life-threatening infections. The report must also include recommendations to improve the program, as well as recommendations to improve stewardship of antimicrobial drugs in healthcare settings.* [Sec. 834]
Guidance on pathogen-focused antibacterial drug development		
No provision.	No provision.	Would require the Secretary, by June 30, 2013, to publish draft guidance that addresses data needs and other approaches for the development of antibacterial drugs to treat serious or life-threatening bacterial infections. The Secretary would be required to finalize guidance by Dec. 31, 2014. [Sec. 835]

Source: CRS analysis of current law, S. 3187 (as passed), and H.R. 5651 (as passed).

Notes: Italics are provided to emphasize differences between the Senate and House bills.

a. FFDCA Sec. 505(v) [21 USC 355(v)] makes certain older antibiotic drugs ineligible for exclusivity. For general information about exclusivity, see CRS Report R41114, *The Hatch-Waxman Act: A Quarter Century Later*, by Wendy H. Schacht and John R. Thomas.

b. For more information about expedited approval processes, see CRS Report RS22814, *FDA Fast Track and Priority Review Programs*, by Susan Thaul.

Expedited Drug Development and Review Processes[23]

Before a drug may be sold in the United States, the Food and Drug Administration (FDA) must approve an application from its manufacturer. The progression to drug approval begins before FDA involvement with, first, basic scientists work in the laboratory and with animals, and, second, a drug or biotechnology company develops a prototype drug. That company must seek and receive FDA approval, by way of an investigational new drug (IND) application, to test the product with human subjects. Those tests, called clinical trials, are carried out sequentially in Phase I, II, and III studies, which involve increasing numbers of subjects. The manufacturer then compiles the resulting data and analysis in a new drug application (NDA). FDA reviews the NDA

[23] Erin Bagalman, Analyst in Health Policy; Susan Thaul, Specialist in Drug Safety and Effectiveness; and Sarah A. Lister, Specialist in Public Health and Epidemiology, prepared this section of the report. For follow-up discussions, contact Susan Thaul.

with three major concerns: (1) safety and effectiveness in the drug's proposed use; (2) appropriateness of the proposed labeling; and (3) adequacy of manufacturing methods to assure the drug's identify, strength, quality, and identity. The Federal Food, Drug, and Cosmetic Act (FFDCA) and associated regulations detail the requirements at each step. Not all reviews and applications follow the standard procedures.

In certain circumstances, FDA regularly uses three formal mechanisms to expedite the development and review process.[24] For a drug for a serious or life-threatening condition, *accelerated approval*[25] and *animal efficacy approval*[26] processes—provided for in regulations—change what is needed in an application when a drug or biological product may provide a meaningful therapeutic benefit over existing treatments. A *fast track product* designation[27]—provided for in law—affects the timing and smoothness of the application process for a drug with the potential to address an unmet medical need. *Priority review*—based in FDA procedures—affects the timing of the review, not the process leading to submission of an application, when FDA determines a drug would address an unmet need.[28]

Provisions in S. 3187 and H.R. 5651 would amend the FFDCA to "help expedite the development and availability to patients of treatments for serious or life-threatening diseases or conditions while maintaining safety and effectiveness standards."[29] They would do so by combining elements of the regulatory *accelerated approval* process and the statutory *fast track product* designation, and creating a new designation—*breakthrough therapy*—for a drug whose preliminary clinical data suggest a possible substantial improvement over existing therapies. **Table 9** describes the Senate and House provisions arrayed generally in relation to current law. Although the provisions all are meant to bring needed drugs to consumers sooner than they would get there otherwise, they focus on different elements of the overall process. One element is the product. Some provisions identify characteristics of the drug, the patient group, or the disease that would make a drug eligible for a designation: a fast track product or a breakthrough therapy. A second element is the interaction between FDA and the drug developer or manufacturer. Some provisions would create administrative processes that could make the development go more smoothly. A third element is the criteria used in assessing evidence of safety and effectiveness. Some provisions would allow different uses of surrogate outcome measures or look to newer scientific methods and tools to better predict clinical benefits. Both bills also include reporting, guidance, and evaluation provisions.

[24] For a discussion of drug development and the Food and Drug Administration (FDA) review process, including these special mechanisms, see CRS Report R41983, *How FDA Approves Drugs and Regulates Their Safety and Effectiveness*, by Susan Thaul.

[25] 21 CFR 314 Subpart H for drugs, and 21 CFR 601 Subpart E for biological products. A second accelerated approval situation addresses drugs whose use FDA considers safe and effective only under set restrictions that could include limited prescribing or dispensing. FDA usually requires postmarketing studies of products approved this way.

[26] The Animal Efficacy Rule allows manufacturers to submit effectiveness data from animal studies as evidence to support applications of certain new products "when adequate and well-controlled clinical studies in humans cannot be ethically conducted and field efficacy studies are not feasible" (21 CFR 314 Subpart I and 21 CFR 601 Subpart H).

[27] FFDCA §506 [21 USC §356]. FDA, "Guidance for Industry: Fast Track Drug Development Programs—Designation, Development, and Application Review," Center for Drug Evaluation and Research and Center For Biologics Evaluation and Research, January 2006.

[28] FDA, "Fast Track, Accelerated Approval and Priority Review," http://www.fda.gov/ForConsumers/ByAudience/ForPatientAdvocates/SpeedingAccesstoImportantNewTherapies/ucm128291.htm.

[29] Sense of Congress, Sec. 901(a) of S. 3187 (as passed) and Sec. 841(a) of H.R. 5651 (as reported).

Table 9. Expedited Drug Development and Review Processes

Current Law	S. 3187 (as passed)	H.R. 5651 (as passed)
Fast track products: designation		
FFDCA Sec. 506 requires the Secretary to facilitate the development and expedite the review of a drug designated a "fast track product," defined as a drug intended for the treatment of a *serious or life-threatening condition* that demonstrates the potential to address unmet medical needs for such a condition. [FFDCA 506(a); 21 USC 356(a)]	Would *replace FFDCA Sec. 506 with new language*, which would change "serious or life-threatening condition" to "*serious or life-threatening disease or condition*." Would specify that the requirement that a drug be intended for treatment of a serious or life-threatening disease or condition and which demonstrates the potential to address unmet medical needs, applies "*whether alone or in combination with one or more other drugs*." [Sec. 901(b)]	The House bill *also would replace FFDCA Sec. 506 with new language*, and contains a substantively identical designation. [Sec. 841(b)]
Accelerated approval: evidence for clinical and surrogate endpoints		
Allows the Secretary to approve an application for *approval of a fast track product* "upon a determination that the product has an effect on a clinical endpoint or on a surrogate endpoint that is reasonably likely to predict clinical benefit." [FFDCA 506(b)(1); 21 USC 356(b)(1)] FDA regulations provide for the "accelerated approval" of drug and biologics applications. [21 CFR 314 Subpart H and 21 CFR 601 Subpart E]	Would expand the expedited approval process to a drug intended for treatment of a serious or life-threatening disease or condition, *including (but not limited to) a fast track product. Would add detail about what constitutes sufficient evidence* for the clinical and surrogate endpoints used in the accelerated approval process. In addition, would explicitly designate this expedited approval process as "accelerated approval." [Sec. 901(b)]	The House bill contains substantively similar provisions, except that the *list of sufficient evidence for endpoints differs in some particulars*, and the bill *would not explicitly designate the process as "accelerated approval."* [Sec. 841(b)]
Accelerated approval: limitations on product approval		
Authorizes the Secretary to impose the following requirements as a condition of *approval of a fast track product:* the sponsor must conduct post-approval studies to validate surrogate and/or clinical endpoints; and the sponsor must submit copies of promotional materials for review by the Secretary at least 30 days prior to dissemination. [FFDCA 506(b)(2); 21 USC 356(b)(2)]	Would allow the Secretary to impose one or both of these limitations on the accelerated approval of *a product (not limited to a fast track product*), although *wording of the requirement regarding post-approval studies is somewhat different from current law.* [Sec. 901(b)]	The House bill contains provisions substantively comparable to those in the Senate bill, although the language *differs in some particulars, such as the explicit mention of pre-submission of promotional materials in both the pre-approval and post-market periods.* [Sec. 841(b)]
Accelerated approval: expedited withdrawal of approval		
Allows the Secretary to expedite withdrawal of approval of a fast track product under certain circumstances. [FFDCA 506(b)(3); 21 USC 356(b)(3)]	Would retain this authority of the Secretary using language comparable to current law, *except that this authority could apply to any product eligible for accelerated approval, not limited to a fast track product.* [Sec. 901(b)]	Also would retain this authority, using language comparable to the Senate bill, *except to refer to "a product approved pursuant to this subsection using expedited procedures," which would not be limited to a fast track product.* (As noted above, the House bill does not explicitly define "accelerated approval.") [Sec. 841(b)]

Current Law	S. 3187 (as passed)	H.R. 5651 (as passed)
Accelerated approval: review of incomplete applications for fast track products		
Requires the Secretary to evaluate for filing, and allows the Secretary to commence review of portions of, an incomplete application for a fast track product, if the Secretary determines (based on preliminary evaluation of clinical data submitted by the sponsor) that the product may be effective. [FFDCA 506(c); 21 USC 356(c)]	As noted above, this subsection would replace FFDCA Sec. 506 in its entirety. However, the Senate bill would retain this provision in current law without any change. [Sec. 901(b)]	As noted above, this subsection would replace FFDCA Sec. 506 in its entirety. However, like the Senate bill, the House bill would retain this provision in current law without any change. [Sec. 841(b)]
Expedited development and approval: dissemination of policy		
Requires the Secretary to develop and disseminate to appropriate persons and organizations a description of the law "applicable to fast track products; and establish a program to encourage the development of *surrogate endpoints that are reasonably likely to predict clinical benefit*" for serious/life-threatening conditions with significant unmet medical needs. [FFDCA 506(d); 21 USC 356(d)]	Would expand upon current law to apply it to *accelerated approval, fast track, and breakthrough products*. Would expand the scope of the program required by current law to encourage the development of "surrogate *and clinical endpoints, including biomarkers, and other scientific methods and tools that can assist the Secretary in determining whether the evidence submitted in an application is reasonably likely to predict clinical benefit*" for serious/life-threatening conditions with significant unmet medical needs. [Sec. 901(b) (application to accelerated approval and fast track products) and Sec. 902 (application to breakthrough therapies)]	Would expand upon current law in the same manner as in the Senate bill. [Sec. 841(b) (application to accelerated approval and fast track products) and Sec. 869 (application to breakthrough therapies)]
Expedited development and approval: rules of construction concerning fast track products, accelerated approval, and breakthrough therapies		
No provision.	Would add two rules of construction regarding accelerated approval: (1) to indicate that FFDCA Sec. 506, as replaced by this section, should not be construed to alter the standards of evidence of safety and effectiveness required for drug approval under FFDCA Sec. 505 or PHSA Sec. 351; and (2) to state that this section would not alter the Secretary's ability to use evidence from other than adequate and well-controlled investigations in order to determine whether an endpoint is reasonably likely to predict clinical benefit. [Sec. 901(b)]	No provision.
Expedited development and approval: guidance		
No provision.	Would require the Secretary to issue draft guidance within 1 year of enactment, issue final guidance within 1 year of the issuance of draft guidance, and amend relevant regulations to conform. Would require the Secretary,	Although phrased differently, the House bill would impose substantively similar requirements, and identical deadlines, regarding guidances and regulations to implement Sec. 841 of this bill,

Current Law	S. 3187 (as passed)	H.R. 5651 (as passed)
	in developing such guidance, to consider issues arising under the accelerated approval and fast track processes for drugs intended to treat rare and very rare diseases. States that the Secretary's failure to issue timely guidances or amend regulations would not affect product reviews under FFDCA Sec. 506 (as amended). [Sec. 901(c)]	although it does not explicitly refer to very rare diseases. This section also contains the same clarification regarding failure of timely action by the Secretary. [Sec. 842]
Expedited development and approval: independent review		
No provision.	Would allow the Secretary to contract with an independent entity to evaluate the expedited approval processes in FFDCA Sec. 506 (as amended) and their impact on the development and availability of innovative treatments for patients suffering from serious or life-threatening conditions. Would require such evaluation (if conducted) to include consultation with regulated industries, patient advocacy and disease research foundations, and relevant academic medical centers. [Sec. 901(d)]	The House bill contains a substantively identical provision. [Sec. 843]
Breakthrough therapies: designation		
No provision.	Would further amend FFDCA Sec. 506 to require the Secretary to expedite the development and review of a drug designated a "breakthrough therapy," defined as a drug intended (alone or in combination with another drug or drugs) to treat a serious or life-threatening disease or condition, and for which preliminary clinical evidence indicates the possibility of substantial improvement over existing therapies. Would allow a sponsor to request breakthrough therapy designation upon or after the submission of an investigational new drug application. Would require the Secretary to make a determination on such designation within 60 calendar days. Would specify actions the Secretary may take to expedite development and review of a drug so designated. [Sec.902(a)]	The House bill contains a substantively identical provision. [Sec. 869]
Breakthrough therapies: reports		
No provision.	Would require the Secretary to submit annual reports to Congress, beginning in FY2013, on the number of requested and approved breakthrough therapy designations, and related actions. [Sec. 902(a)] Would require GAO, within 3 years of enactment, to assess the impact of the	The House bill contains a substantively identical provision. [Sec. 869(a) and Sec. 869(c)]

Current Law	S. 3187 (as passed)	H.R. 5651 (as passed)
	breakthrough designation and process on the availability of treatments for serious or life-threatening conditions. [Sec. 902(c)]	
Breakthrough therapies: guidance		
No provision.	Would require the Secretary to: issue draft guidance regarding breakthrough therapies within 18 months of enactment; issue final guidance within 1 year of the closing of the draft guidance comment period; and amend regulations to conform, if necessary, within 2 years of enactment, as specified. [Sec. 902(b)]	The House bill contains a substantively identical provision. [Sec. 869(b)]

Source: CRS analysis of current law, S. 3187 (as passed), and H.R. 5651 (as passed).

Drug Shortages[30]

Since 2005, FDA, clinicians, pharmacists, and patients have noted more frequent drug shortages—when the local or nationwide supply of a particular dosage is inadequate to meet demand. Recent shortages have clustered around generic sterile injectable drugs used during surgery or hospital care, although shortages have affected brand-name products and oral tablets for a wide range of diseases and conditions.[31]

Immediate causes of shortages include: (1) manufacturing quality problems (such as contaminants); (2) interruption in supply of ingredients; (3) unanticipated increase in demand (e.g., the unavailability of another product for the same condition, recent attention to an off-label use, or approval of an additional indication or user population); (4) business decisions by individual firms (e.g., to cut back on the number of facilities dedicated to a particular drug, or to shut down during renovation); and (5) unanticipated weather, accident, or other event.[32] Less clear is why the rate of shortages (or public awareness of them) is increasing now.

Market concentration and a global supply chain, along with manufacturing capacity constraints, the complex process of drug production, inventory practices, and pricing, act as underlying causes, many believe, of drug shortages. Many of sterile injectable drugs are made by few producers in specialized facilities. For example, when one of two manufacturing facilities goes off-line for any reason, the remaining facility may be able to meet the total demand for a while, but not indefinitely. Patterns of practice in the drug distribution industry, such as just-in-time inventories, leave little back-up capacity from warehouses.[33]

[30] Susan Thaul, Specialist in Drug Safety and Effectiveness, prepared this section of the report.

[31] Food and Drug Administration (FDA), "Current Drug Shortages," http://www.fda.gov/Drugs/DrugSafety/DrugShortages/ucm050792.htm.

[32] FDA, "A Review of FDA's Approach to Medical Product Shortages," October 31, 2011, http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Reports/UCM277755.pdf; Government Accountability Office (GAO), "Drug Shortages: FDA's Ability to Respond Should Be Strengthened," Report to Congressional Requesters, GAO-12-116, November 2011, http://gao.gov/assets/590/587000.pdf.

[33] Department of Health and Human Services (HHS), "Economic Analysis of the Causes of Drug Shortages," ASPE Issue Brief, Office of Science and Data Policy, Office of the Assistant Secretary for Planning and Evaluation, October (continued...)

It is not always feasible for other manufacturers to add production capacity to ease a shortage. First, it takes time to construct new facilities. Second, FDA must approve the manufacturing process and recordkeeping along with product specifications. Third, a manufacturer must decide to use the new or existing facility for the drug in shortage rather than for another product that may yield greater profit or better fit within the company's business plan.

FDA has acted within its current authority by asking both sole source and other firms to increase production, exercising flexibility through regulatory discretion (e.g., allowing the importation), expediting review, and communicating with the Drug Enforcement Administration (DEA) about quotas of controlled substances.[34] An Executive Order directed FDA to use all tools to require that manufacturers give advance notice of manufacturing interruptions, to expedite applications, and to work with the Department of Justice (DOJ) to address instances of price gouging, for example, when pharmacies turn to supplies outside their routine distribution channels.[35] FDA and GAO analyses suggested immediate steps to increase notification, increase staffing, develop legislation to require notification, and communicate with the public and within FDA. They suggested longer term steps such as using databases to identify factors that help prevent or mitigate shortages, identifying manufacturing quality issues and having backup plans, using sentinel reports from providers to identify imminent shortages, and encouraging wholesaler transparency. Others have suggested requiring pedigrees and data systems to both track the availability and verify the legitimacy of shipments; and providing incentives to manufacturers. Some have suggested that reimbursement and purchasing policies—for Medicare, Medicaid, other public programs—as well as the interplay of pharmaceutical and medical care billing for injectable oncology drugs may contribute to drug shortages; these possibly reasonable theories have not yet been empirically demonstrated.

Most pending legislation in the 112th Congress has focused on notification requirements,[36] although at least one Member is developing a plan that could involve Medicare and Medicaid payment policies.[37] The provisions in S. 3187, as passed in the Senate, focus on expanding the scope of the notification requirements, authorizing expedited inspections and review, and requiring information collection and use, along with studies of the causes and extent of shortages. H.R. 5651 provisions, as passed by the House, focus on notification, a drug shortage list with reasons and estimated duration as determined by the Secretary, coordination with the Attorney General regarding production quotas, and Attorney General actions and report. These provisions are summarized and compared in **Table 10**.

(...continued)

2011, http://aspe.hhs.gov/sp/reports/2011/DrugShortages/ib.pdf.

[34] FDA, "A Review of FDA's Approach to Medical Product Shortages," October 31, 2011, http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Reports/UCM277755.pdf.

[35] The White House, "Executive Order 13588—Reducing Prescription Drug Shortages," Office of the Press Secretary, October 31, 2011, http://www.whitehouse.gov/the-press-office/2011/10/31/executive-order-13588-reducing-prescription-drug-shortages.

[36] See S. 296, H.R. 2245, and H.R. 3839.

[37] "Hatch Floats Economic Drug Shortage Solutions Not In Senate HELP Draft," posted April 19, 2012, InsideHealthPolicy.com, http://insidehealthpolicy.com/201204192396433/Health-Daily-News/Daily-News/hatch-floats-economic-drug-shortage-solutions-not-in-senate-help-draft/menu-id-212.html. The article includes a link to a discussion draft (header on undated draft is "KER12226, S.L.C.").

Table 10. Drug Shortages

Current Law	S. 3187 (as passed)	H.R. 5651 (as passed)
Required notification of interruption in supply		
Current law requires a manufacturer that is the *sole manufacturer* of a drug that is *life-supporting, life-sustaining, or intended for use in the prevention of a debilitating disease or condition* to notify the Secretary at least 6 months before the date of a *discontinuance* in the manufacture of that drug. The requirement applies to drugs with *approved marketing applications*. It *excludes* a product that was originally derived from human tissue and was replaced by a recombinant product. The law includes conditions under which the notification period *may be reduced*. It also requires the Secretary to *distribute discontinuation information* to appropriate physician and patient organizations. [FFDCA 506C; 21 USC 356c]	This section would amend current law to: (1) remove the word "sole," so that the law would apply to all manufacturers of certain drugs; (2) delete the restriction to drugs approved under the FFDCA; (3) add certain types of drugs—sterile injectable products and drugs used in emergency medical care or during surgery; (4) exempt certain additional drugs—radio-pharmaceutical drug products and products derived from human plasma protein—from the notification requirement, including drugs designated by the Secretary; (5) require notification of both a permanent discontinuance and a manufacturing interruption that could lead to meaningful disruption of the U.S. supply of that drug; and (6) allow manufacturers to notify the Secretary as soon as practicable if they cannot comply with the advance notice requirement. [Sec. 1001(a)]	This section is similar to the Senate provision, with differences noted below: (1) similar to Senate provision; (2) similar to Senate provision; specifies that this would apply to a manufacturer of a drug subject to FFDCA 503(b)(1), which refers to drugs that require a prescription; (3) no House provision; (4) similar to Senate provision, phrased differently; (5) similar to Senate provision; would also require the reason for the discontinuation or interruption; and (6) similar to Senate provision. [Sec. 901(a)]
Confidentiality		
The Freedom of Information Act "does not apply to matters that are ... trade secrets and commercial or financial information obtained from a person and privileged or confidential." [5 USC 552(b)(4)] Current law establishes criminal penalties for government employees who disclose confidential information acquired through their work. [18 USC 1905]	No provision would explicitly cover the entire drug shortages section of the Senate bill. However, the bill includes a provision similar to House bill Sec. 901(a) that would apply to a required GAO report on market conditions; see below. [Sec. 1001(d)]	(7) Would specify that "Nothing in this section shall be construed as authorizing the Secretary to disclose any information that is a trade secret or confidential information subject to section 552(b)(4) of title 5, United States Code, or section 1905 of title 18, United States Code." [Sec. 901(a)]
Failure to meet requirements		
No provision.	No provision.	Would provide procedures and timeframe for the Secretary to take when a person fails to submit required information in the required timeframe. [Sec. 901(a)]
Expedited inspections and reviews		
No provision in FFDCA 506C. The Secretary has the general authority to prioritize inspection and review schedules.	Would explicitly authorize the Secretary to expedite establishment inspections and review of applications and supplements that could help mitigate or prevent a "shortage," as defined in this section. [Sec. 1001(a)]	Would require the Secretary to expedite the review of a major manufacturing change application if the manufacturer certifies that the change "may prevent or alleviate a discontinuance or interruption"

Current Law	S. 3187 (as passed)	H.R. 5651 (as passed)
		unless the Secretary determines the certification was made in bad faith. [Sec. 904] Would not explicitly address inspections or other review situations.
Task force and plan		
No provision.	Would require the Secretary to establish a task force to enhance the Secretary's response to shortages and create a strategic plan to enhance interagency coordination, address drug shortage possibilities when initiating regulatory actions, communicate with stakeholders, and consider the impact of drug shortages on research and clinical trials. [Sec. 1001(a)]	No provision.
Assess and communicate potential effects of actions on shortages		
No provision.	Would require the Secretary, before any enforcement action or issuance of a warning letter that could reasonably be anticipated to lead to a meaningful disruption (as defined in this title) in the U.S. supply of a drug, to communicate with FDA drug shortage experts and, if the action or letter could reasonably cause or exacerbate a shortage, to evaluate risks of a shortage and the risks associated with the violation. [Sec. 1001(a)]	No provision.
Reporting		
No provision.	Would require a mechanism for certain persons to report shortages and would mandate the Secretary 's maintenance of records with specified information on shortages. Would require the Secretary to report to Congress with a summary of such information. [Sec. 1001(a)]	No provision.
No provision.	Would also authorize the Secretary to retain a third party to conduct a trend analysis related to shortages. [Sec. 1001(a)]	No provision.
No provision.	No provision.	Would require the Secretary to report to Congress no later than 18 months after enactment and annually thereafter on FDA communication procedures, efforts to expedite review coordination with DEA, other specified details of FDA actions, and the Secretary's plan for addressing shortages in the upcoming year. [Sec. 906]

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Final regulation		
No provision.	Would direct the Secretary finalize an implementing regulation within 18 months of enactment. [Sec. 1001(a)]	Similar provision. Would also specify recommended content of the regulations. [Sec. 901(b)]
No provision.	Would authorize the Secretary to apply, by regulation, this section to biological products, and would require the Secretary to consider if the notification requirement for vaccines could be met through the Centers for Disease Control and Prevention (CDC) vaccine shortage notification program. [Sec. 1001(a)]	No provision.
Effect of notification		
No provision.	According to this paragraph, submission of a notification of a permanent discontinuance or interruption in the manufacture of a drug that could lead to a shortage would not be construed as an admission that a product was in violation of the FFDCA or that the product was promoted or marketed for an unapproved use or indication. [Sec. 1001(b)]	No provision.
Internal review		
No provision.	Would require the Secretary, within 2 years of enactment, to conduct an internal review of regulations, guidances, policies, and practices related to the manufacture of human drugs to identify their impacts on shortages. [Sec. 1001(c)]	No provision.
GAO report		
No provision.	Would require GAO, in consultation with the HHS Secretary, the HHS Office of the Inspector General, the Attorney General, and the Chair of the Federal Trade Commission, to report on topics to include stockpiling and significant price increases, number of manufacturers, pricing structure, and federal reimbursement, among other specified content. [Sec. 1001(d)(1,2)] Would specify that "Nothing in this subsection alters or amends section 1905 of title 18, United States Code, or section 552(b)(4) of title 5, United States Code," regarding trade secret and confidential information. [Sec. 1001(d)(3)]	Would require GAO, in consultation with relevant stakeholders, to study the cause of drug shortages and to recommend ways to prevent or alleviate shortages. It specifies questions for GAO to consider, such as characteristics of drugs, pricing structure including federal reimbursement, number of manufacturers, federal actions, and healthcare provider responses. [Sec. 905]

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Attorney General report		
No provision.	No provision.	Would require the Attorney General, within 6 months of enactment and annually thereafter, to report to Congress on drug shortages to include the number of requests received for increased quotas and actions taken and their reasons; coordination between DEA and FDA; and identification of controlled substances that the Secretary determined to be in shortage. [Sec. 907]
Repackaging guidance		
No provision.	Would require the Secretary to issue guidance to clarify FDA policy regarding hospital pharmacies' repackaging and transferring of repackaged drugs within a common health system during a shortage. [Sec. 1001(e)]	Would add a new FFDCA Sec. 506E, "Hospital repackaging of drugs in shortage," to exclude from establishment registration requirements of FFDCA Sec. 510 a hospital that repackages a drug on the FDA drug shortage list for transfer to another hospital in the same health system. This section would terminate when the Secretary issues final guidance clarifying FDA policy on such repackaging. [Sec. 908]
Drug shortage list		
No provision. (FDA does maintain a webpage that lists current drug shortages and includes name of drug and manufacturer and the reason for the shortage as reported by the manufacturer.)	No provision.	Would add a new FFDCA Sec. 506D, "Drug Shortage List," that would require the Secretary to maintain an up-to-date list of U.S. drug shortages and specifies that the list include names of drug and manufacturer, reason for shortage as determined by the Secretary, and estimated duration as determined by the Secretary. [Sec. 902] Would require the Secretary to make the list public unless it conflicted with laws regarding trade secrets and confidential information or the Secretary determined that public disclosure of shortage information would adversely affect the public's health. [Sec. 902]
Attorney General coordination, action, and reporting		
Under the Controlled Substances Act (CSA), each year the Attorney General (AG) must establish production quotas for controlled substances, and each year sets a quota for each manufacturer based	No provision.	Would amend FFDCA Sec. 506C to require the Secretary to determine whether a drug that a manufacturer notifies the Secretary is a controlled substance subject to a quota under CSA Sec. 306. If the

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on specified considerations including "the manufacturer's production cycle and inventory position, the economic availability of raw materials, yield and stability problems, emergencies such as strikes and fires, and other factors." [CSA 306(a,c); 21 USC 826(a,c)] CSA allows a manufacturer to apply for a increase of the annual quota. [CSA 306; 21 USC 826(e)]		Secretary then determined it necessary, would require the Secretary to notify the AG, request that the AG increase production quotas for the drug or ingredient, as necessary, to address the shortage. If the AG determined that quota change is not necessary, the AG would be required to provide written explanation which the Secretary would be required to make available to the public. [Sec. 901(e)] Would amend CSA Sec. 306 to require the AG to review a request from a manufacturer for an increase in the quota of a drug or ingredient in shortage and to increase the quota or provide written response with reasons otherwise, which the Secretary would be required to make publicly available. [Sec. 903] See also "Attorney General report" above. [Sec. 907]

Source: CRS analysis of current law, S. 3187 (as passed), and H.R. 5651 (as passed).

Medical Gas Regulation[38]

Although medical gases are considered to be prescription drugs under the FFDCA, FDA has exercised regulatory discretion in not requiring new drug applications or imposing user fees on companies. FDA oversees medical gases through current good manufacturing practice (CGMP) regulations (21 CFR parts 210 and 211) and guidance. Medical gas manufacturers sought an approval pathway in law to avoid certain trade and other problems associated with their products being considered "unapproved."[39] Both the Senate and House bills propose a means for the Secretary to approve medical gases that meet requirements through a certification process, which would not confer market exclusivity or require the payment of user fees. The applicable provisions are summarized in **Table 11**.

[38] Sarah A. Lister, Specialist in Public Health and Epidemiology, prepared this section of the report.

[39] Nanci Bompey, "FDA, Industry Agree To Put Medical Gas Under Current Drug Regs Without Fees," *FDA Week*, May 3, 2012.

Table 11. Medical Gas Regulation

(no current law)

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The Senate bill would essentially codify the current regulatory approach. Would define a "*designated medical gas product*" as oxygen; nitrogen; nitrous oxide; carbon dioxide; helium; carbon monoxide; medical air; and any other medical gas product designated by the Secretary. Would establish a process*, effective upon enactment*, whereby the Secretary would be required to certify medical gas products pursuant to satisfactory application by a company, as specified. A certified product (or mixture) would be deemed to have in effect an approved new drug application, subject to applicable post-approval requirements, for a list of specified indications. However, such certification would not confer an exclusivity period or require payment of user fees. Specified labeling would be required. The Secretary could withdraw, suspend, or revoke certification as per current authority for regulation of drugs. A prescription would generally be required, with specified exceptions for oxygen use. [Sec. 1111]	The House bill is substantively the same as the Senate bill with regard to most provisions, with exceptions as noted below. The House bill refers to a "*designated medical gas*;" all other definitions of gases and eligible indications are identical to the Senate bill. The House bill would require the certification process to be *in effect within 180 days of enactment.* [Sec. 821]
The Secretary would be required to review and report on current regulation within 18 months of enactment, amend them as needed, and finalize them within 4 years of enactment. [Sec. 1112]	The House bill includes a comparable provision regarding regulations. [Sec. 822]
The provisions above would not apply to any drug approved prior to May 1, 2012, or any medical gas listed in this bill that is approved on or after May 1, 2012 for an indication other than those listed in Sec. 1111 of this bill, above. [Sec. 1113]	The House bill states the two limitations present in the Senate bill, and contains an additional subsection stating that *provisions also would not apply to an unlisted medical gas certified by the Secretary if it was not used for an indication deemed appropriate by the Secretary.* [Sec. 823]

Source: CRS analysis of S. 3187 (as passed) and H.R. 5651 (as passed).

Notes: Italics are used to emphasize differences between bills.

Miscellaneous Provisions Regarding Human Drug Regulation[40]

The following additional drug-related provisions are summarized and compared in **Table 12**:

- Independent assessment of drug approval processes;
- Drugs for rare diseases;
- Accessibility of prescription information for the blind and visually impaired;
- Risk-benefit assessment framework for new drug applications (NDAs);
- National Academies study on medical innovation inducement;
- Reauthorization of grants and contracts for development of orphan drugs;
- Reporting of demographic subgroups in clinical trials data;

[40] Many members the team contributed to this section of the report. For follow-up discussions, contact Susan Thaul, Specialist in Drug Safety and Effectiveness.

- Reauthorization of exclusivity for single-enantiomer drugs;
- Prescription drug abuse;
- Risk evaluation and mitigation strategies (REMS) and drug access for development;
- Extension of period before forfeiting marketing exclusivity for an ANDA;
- FDA actions and deadlines on petitions; and
- Assessment and modification of approved REMS.

Table 12. Human Drug Regulation: Miscellaneous

Current Law	S. 3187 (as passed)	H.R. 5651 (as passed)
Independent assessment of drug approval processes		
No provision.	Would require the Secretary to contract with a private, independent consulting firm to conduct a comprehensive assessment of the process for the premarket review of drug applications. The two-phase assessment would include participation of FDA and manufacturers, specified content, and a requirement that the Secretary analyze recommendations and develop and implement a corrective action plan. [Sec. 723]	No provision.
Rare diseases and genetically targeted treatments: consultation with external experts		
Current law addresses drugs for rare diseases or conditions. Among other things, upon designating a new drug or biological product candidate as a drug to diagnose or treat a rare disease or condition (according to specified protocols), the Secretary must, upon a sponsor's request, provide information about clinical and non-clinical investigations that may be needed for approval. This provision does not specifically address the use of external experts in the premarket period, however. [FFDCA 525; 21 USC 360aa] Current law defines criteria and requirements, including those regarding conflicts of interest, for special government employees. [18 USC 202]	Would add a new FFDCA section to require the Secretary to develop and maintain a list of external experts with whom to consult regarding specified topics in the review of new drugs and biological products for rare diseases, and drugs and biological products that are genetically targeted, when such consultation is necessary because the Secretary lacks the requisite expertise. Would allow the external experts to be considered special government employees. [Sec. 903]	The House bill contains a provision substantively identical to that in the Senate bill. [Sec. 868]
Rare diseases and external consultation: protection of proprietary information		
Current law has many provisions addressing confidentiality and protection of trade secrets, but none specifically addresses consultation with external experts on rare diseases.	Would state that "nothing in this section shall be construed to alter the protections offered by laws, regulations, and policies governing disclosure of confidential commercial or trade secret information…." [Sec. 903]	The House bill includes the same rule of construction as in the Senate bill. *In addition, it would prohibit the Secretary from disclosing any confidential commercial or trade secret information to an expert consulted under this section without the sponsor's*

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		written consent, unless the expert is a special government employee or the disclosure is otherwise authorized by law. [Sec. 868]
Rare diseases and external consultation: rules of construction and review time		
No provision.	No provision.	The House bill would require the appropriate FDA center or division director, prior to a consultation with an external expert, to determine either that the sponsor authorized the consultation, or that the consultation will facilitate review, address deficiencies in the application, and increase the likelihood of an approval decision in the current review cycle. [Sec. 868]
No provision.	Would state that this section would not: (1) limit the ability of the Secretary to continue consultations that were authorized prior to enactment; (2) create a legal right of the expert or stakeholder for a consultation or meeting with the Secretary; (3) affect goals and procedures agreed upon under user fee authority; or (4) increase the number of review cycles in effect before enactment. [Sec. 903]	The House bill contains the same rules of construction. [Sec. 868]
Rare diseases and genetically targeted therapies: consultation with stakeholders		
No provision.	Would require the Secretary to ensure that opportunities exist, as appropriate, for consultation with stakeholders on specified topics related to new drugs and biological products that are for rare diseases or that are genetically targeted. [Sec. 903]	The House bill contains a substantively identical provision. [Sec. 868]
Accessibility of prescription information for the blind and visually impaired: best practices		
No provision.	Would require the Architectural and Transportation Barriers Compliance Board to convene a stakeholder working group to develop best practices on access to information on prescription drug labels for individuals who are blind or visually impaired, within 1 year of enactment. Would allow the best practices to be made publicly available. Would require the working group to consider challenges to adoption of best practices by pharmacies with 20 or fewer retail locations. Would include a rule of construction that the best practices would not be construed as guidelines or standards. [Sec. 904]	No provision.

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Accessibility of prescription information for the blind and visually impaired: GAO study		
No provision.	Would require a GAO study of the extent to which pharmacies are utilizing best practices and the extent to which barriers to accessible information on prescription drug container labels for blind and visually impaired individuals continue; would require the study to begin 18 months after completion of the development of best practices and to be submitted to Congress no later than September 30, 2016. [Sec. 904]	No provision.
Risk-benefit assessment framework for a new drug application (NDA)		
Defines criteria for evaluating a new drug application (NDA). [FFDCA 505(d); 21 USC 355(d)]	Would require the Secretary to "implement a structured risk-benefit assessment framework in the new drug approval process to facilitate the balanced consideration of benefits and risks, a consistent and systematic approach to the discussion and regulatory decisionmaking, and the communication of the benefits and risks of new drugs." Would not "alter the criteria for evaluating an application for premarket approval of a drug." [Sec. 905]	Would not change current law.
National Academies study: medical innovation inducement		
No provision.	Would require the Secretary to contract with the National Academies to conduct an evaluation of the feasibility and possible consequences of using innovation inducement prizes to reward successful medical innovations. Would require the National Academies to submit the report to the Secretary no later than 15 months after enactment. [Sec. 906]	No provision.
Grants and contracts for development of orphan drugs: reauthorization		
Among other provisions, the Orphan Drug Act authorizes the Secretary to provide grants and contracts to public and private entities to defray the costs of qualified testing used for orphan drug development. To qualify, the costs must be incurred both after the Secretary designated the product as a drug for a rare disease or condition and before the entity submitted the new drug application or biologics license application to FDA. [21 USC 360ee(b)(1)]	Would eliminate the requirement that the costs be incurred after designation as a drug for a rare disease or condition. [Sec. 907(b)]	The House bill contains a substantively identical provision. [Sec. 870(a)]

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Authorizes the appropriation of $30 million for grants and contracts for each of FY2008-FY2012. [21 USC 360ee(c)]	Would reauthorize the appropriation of $30 million for each of FY2013-FY2017. [Sec. 907(a)]	The House bill contains a substantively identical provision. [Sec. 870(b)]
Reporting of demographic subgroups in clinical trials and data analysis in medical product applications		
No provision.	Would require the Secretary, within 1 year, to publish on the FDA website and provide to Congress a report that addresses the extent to which demographic subgroups (specified as sex, age, race and ethnicity) participate in clinical trials and are included in safety and effectiveness data for applications to the FDA for drugs, biological products, and devices. [Sec. 908(a)] Would require the Secretary, within 1 year after the publication of this report, to publish on the FDA website and provide to Congress an action plan. Required elements of the plan would include recommendations to improve the completeness and quality of demographic data on sex, age, race and ethnicity and provide recommendations to improve the public availability of this data to patients, healthcare providers, and researchers. [Sec. 908(b)]	No provision.
Approval and exclusivity for drugs containing single enantiomers; reauthorization		
An applicant for a non-racemic drug that contains, as an active ingredient, a single enantiomer that is contained in an approved racemic drug, may elect to have the single enantiomer not be considered the same active ingredient as in the approved drug (under certain conditions), thereby permitting a separate exclusivity period. Among the required conditions, *approval of the enantiomer could not rely on investigations that were part of the approval of the racemic mixture*. This election is available for *applications submitted before October 1, 2012*. [FFDCA 505(u); 21 USC 355]	Would reauthorize this provision for *applications submitted before October 1, 2017*. Would clarify that in order for the enantiomer to be considered a different drug, its approval could not rely on *"clinical" investigations* that were part of the approval of the racemic mixture. [Sec. 1101]	Also would also reauthorize this provision for *applications submitted before October 1, 2017. Would not add the clarification re: "clinical" investigations.* [Sec. 861]
Prescription drug abuse		
No provision.	Would require the Secretary to "review current federal initiatives and identify gaps and opportunities with respect to ensuring the safe use *and disposal* of prescription drugs with the potential for abuse." [Sec. 1124(a)]	The House bill provision is similar to that in the Senate bill, but refers only to "*safe use*" rather than "*safe use and disposal*" of prescription drugs. [Sec. 866(a)]
No provision.	Would require the Secretary, within 1 year of enactment, to *post on the*	The House bill provision is similar to that in the Senate bill, with two

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	FDA website a report on the findings of the review above, to include *findings and recommendations* on how to use and build upon federal data sources, disseminate best practices and develop education tools. [Sec. 1124(b)]	differences: (1) the House bill provision specifies that the report be *issued to Congress, (rather than posted on the FDA website)*, and (2) the House bill provision states that the report is to include "*recommendations*," rather than "*findings and recommendations*." [Sec. 866(b)]
No provision.	Would require the Secretary, within 6 months of enactment, to promulgate guidance on the development of "*abuse-deterrent*" drug products. [Sec. 1124(c)]	The House bill provision is similar to that in the Senate bill, but refers to *"tamper-deterrent"* rather than *"abuse-deterrent"* drug products. [Sec. 866(c)]
No provision.	Would require the Secretary, within 1 year of enactment, to "seek to enter into an agreement with the Institute of Medicine to conduct a study and report on prescription drug abuse," that will: evaluate trends; assess opportunities to inform and educate the public, patients, and health care providers; and identify potential barriers, if any, to prescription drug monitoring program participation and implementation. [Sec. 1124(d)]	No provision.
Risk evaluation and mitigation strategies (REMS) and drug access for development		
The Secretary may require a risk evaluation and mitigation strategy (REMS) for an approved drug that requires the manufacturer to institute one of more elements to assure safe use (ETASU), a restriction on distribution or use. An ETASU could require, for example: special certification of health care providers, pharmacies, or healthcare settings that dispense; that the drug must be dispensed to patients only in certain healthcare settings, such as hospitals; and specified tests, monitoring, or registry requirements for patients. [FFDCA 505-1(f)(3); 21 USC 355-1(f)(3)]	Would require a REMS with an ETASU to include an additional element to prohibit a manufacturer from citing an ETASU to prohibit or otherwise limit the supply of a "covered drug" (defined as an approved drug or licensed biologic subject to a REMS with an ETASU) to a drug developer who would use the covered drug for testing to support a generic drug application. The Secretary would have to provide a written notice authorizing the supply of the covered drug to the developer following the procedure proposed in this provision, unless the Secretary directs otherwise based on specified reasons.	Would not change current law.
The Federal Trade Commission (FTC) Act [15 USC 41-58] authorizes the FTC to prevent unfair methods of competition, among other things. The Sherman Act [15 USC 1-7] addresses, among other things, restraint of trade or commerce.	Would require (1) consideration and timely response by Secretary to a request by an eligible drug developer; (2) written notice from the Secretary to both the generic developer and the holder of the approved marketing application [usually the brand-name manufacturer], regarding conditions and, when involving bioequivalence or other clinical test, protocols regarding protections to assure	

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	comparable safe use as would occur under a REMS ETASU; and (3) compliance of the eligible drug developer with applicable laws and regulations. Would make it a violation of a REMS for the application holder to restrict the sale of a covered drug to a developer. Would require the Secretary to notify congressional committees within 30 days of becoming aware of a holder's restricting sale after receipt of written authorizing notice. Would establish that the application holder would not be liable for a claim related to the developer's testing of the covered drug (unless the holder of the application for a covered drug and the eligible developer are the same entity). Would require the eligible drug developer to certify that the developer (1) will comply with all conditions and protocols required by the Secretary and (2) intends to submit an application to the FDA in support of which it will test the covered drug. States that this section should not be construed to affect the authority of the Federal Trade Commission to enforce antitrust statutes, including the FTC Act, the Sherman Act, or any other statute under such Commission's jurisdiction. [Sec. 1131]	
Extension of period before forfeiting the 180-day marketing exclusivity of an ANDA		
When filing an abbreviated new drug application (ANDA), the applicant submits a certification regarding the patent status of the referent new drug product. A Paragraph IV certification asserts that the patent is invalid or will not be infringed by the manufacture, use, or sale of the drug for which the ANDA is submitted. [FFDCA 505(j)(2)(A)(vii)(IV); 21 USC 355(j)(2)(A)(vii)(IV)] Current law allows an applicant 30 months from the filing of an ANDA to obtain tentative approval until forfeiting the 180-day exclusivity period to being the first generic to market. [FFDCA 505(j)(5)(D)(i); 21 USC 355(j)(5)(D)(i)]	Would not change current law.	Would change the period for a first applicant who filed or amended an application with a Paragraph IV certification up to 30 months before enactment: from 30 months to 45 months from when the application was filed or amended. This extended period would decrease in 3 month increments annually beginning on October 1, 2013 (45 months, through October 1, 2015 (36 months). For applications filed on or before the date of enactment and amended between the date of enactment and September 30, 2017, the period would be 30 months, as in current law. [Sec. 862]

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Final agency action on petitions		
FFDCA Sec. 505(q) addresses delays in approvals of pending FFDCA Sec. 505(b)(2) new drug applications (investigations not conducted by or for the applicant) and ANDAs based on the Secretary's review of certain petitions submitted with a statutorily-specified certification or verification. FFDCA Sec. 505(q) provides that the Secretary must not delay approval of these two types of applications because of a request to take action related to the application, unless the request is in the form of a citizen petition or a petition for a stay of action and the Secretary determines, upon reviewing the petition, that a delay is necessary to protect the public health. The Secretary must take final agency action (e.g., denial of the petition) within 180 days of when the petition is submitted. This 180-day time period must not be extended for any reason, including (1) a determination that a delay is necessary to protect the public health; (2) the submission of comments on the petition or supplemental information provided by the petitioner; or (3) the consent of the petitioner. The statute further provides that the Secretary must be considered to have taken final agency action on a petition if, within the 180-day period, the Secretary makes a final decision within the meaning of 21 C.F.R. 10.45(d), which addresses judicial review and exhaustion of administrative remedies. Alternately, the Secretary must be considered to have taken final agency action on a petition if the 180-day time period expires without the Secretary having make a final decision.	Would not change current law.	Would make the entirety of FFDCA Sec. 505(q) applicable to applications for licensure of biological products under 351(k) of the Public Health Service Act (42 USC 262(k)). Would reduce the timeframe in current law for FFDCA Sec. 505(b)(2) new drug applications and for ANDAs by 30 days, to 150 days. Therefore, the Secretary would be required to take final agency action within 150 days of when a citizen petition or a petition for a stay of action is submitted. The Secretary would not be able to extend this 150 day time period for any reason, including the three listed in the statute. [Sec. 863]
Deadline on certain petitions		
One of the many reasons that the FDA may not approve an ANDA is the Secretary's determination that the listed drug has been withdrawn from sale for safety or effectiveness reasons. Under 21 C.F.R. 314.161, the Secretary must make the determination that a listed drug has been voluntarily withdrawn for safety or effectiveness reasons at any time after the drug has been voluntarily	Would not change current law.	Would add a new provision requiring the Secretary to issue a final, substantive determination on either type of petition submitted under 21 C.F.R. 314.161(b) within 270 days after the date the petition is submitted. This amendment would apply to petitions submitted on or after the date of enactment. [Sec. 864]

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withdrawn from sale, but must make the determination (1) before approving an ANDA that refers to the listed drug; (2) whenever a listed drug is voluntarily withdrawn from sale and ANDAs that referred to the listed drug have been approved; and (3) when a person submits 1 of 2 types of petitions for such a determination; (1) a citizen petition; or (2) a petition for the FDA Commissioner to issue, amend, or revoke a regulation or order, or to take or refrain from taking any other form of administrative action. The petition must contain all evidence available to the petitioner concerning the reason that the drug is withdrawn from sale.		
Risk evaluation and mitigation strategies (REMS) assessment and modification		
The Secretary may require, under specified conditions, a risk evaluation and mitigation strategy (REMS) at the time of a new application, after initial approval or licensing when a new indication or other change is introduced, or when the Secretary becomes aware of new information and determines a REMS is necessary. Any approved REMS must include a timetable of assessments. [FFDCA 505-1(g); 21 USC 355-1(g)]	Would not change current law.	Would amend requirements and procedures concerning assessments of approved REMS and their modification. Among the changes are those addressing timeframes for action by the Secretary on a proposed modification: in general, the Secretary must review or act within 180 days from receipt; and within 60 days from receipt if the modification is minor or relates to a safety label change.
The REMS process includes required reviews of approved REMS at specified times initially and then as the Secretary determines, as well as detailed procedures for the review of both proposed REMS and required or voluntary assessments or modifications. [FFDCA 505-1(h); 21 USC 355-1(h)]		Would also require the Secretary, within 1 year of enactment, to issue guidance describing what types of REMS modifications would be considered to be minor. [Sec. 867]

Source: CRS analysis of current law, S. 3187 (as passed), and H.R. 5651 (as passed).

Advisory Committees[41]

Currently, the Secretary is required to consider potential conflicts of interest in appointing persons to FDA advisory committees.[42] The Secretary must "review the expertise of the individual and the financial disclosure report filed by the individual pursuant to the Ethics in Government Act of 1978 … so as to reduce the likelihood that an appointed individual will later require" one of two written waivers under the criminal financial conflict of interest statute,[43] or a waiver under FDA's conflict of interest waiver provision,[44] in order to serve at advisory committee meetings.[45]

Under the criminal financial conflict of interest statute, advisory committee members (whether they are special or regular government employees) are prohibited from participating "personally and substantially … through decision, approval, disapproval, recommendation, the rendering of advice … or otherwise" if they have a financial interest.[46] Advisory committee members are also prohibited from participating if any of the following have a financial interest: the member's spouse; minor child; general partner; organization in which the member serves as an officer, director, trustee, general partner or employee; or any person or organization with whom he is negotiating or has any arrangement concerning prospective employment.[47]

However, the criminal financial conflict of interest statute has several waiver provisions. The first of two specifically referenced in FFDCA Sec. 712 allows for a waiver if the advisory committee member fully discloses the financial interest and the official who appoints the member makes a written determination, in advance, that the financial "interest is not so substantial as to be deemed likely to affect the integrity of the services which the Government may expect from such officer or employee."[48] The second wavier allows the official responsible for the advisory committee member's appointment, after reviewing the financial disclosure report, to make a written certification "that the need for the individual's services outweighs the potential for a conflict of interest created by the financial interest involved."[49]

The FFDCA has its own, additional prohibition and waiver for conflicts of interest. Under the current FFDCA Sec. 712(c)(2)(A), any member of an advisory committee would be prohibited from participating in any "particular matter" in an advisory committee meeting in which such member, or an immediate family member of such member, has a "financial interest that could be affected by the advice given to the Secretary with respect to such matter."[50] The HHS Secretary

[41] Vanessa K. Burrows, Legislative Attorney, prepared this section of the report.

[42] FFDCA § 712(b)(2). Persons appointed to serve on a federal advisory committee to provide independent information and advice to the government, whether compensated or not, may in many instances because of that service be considered "employees of the federal government" and, if they serve on a part-time or intermittent basis, as "special government employees." *See* 18 U.S.C. § 202. As regular or "special government employees," such individuals come within the scope of federal conflict of interest laws and regulations.

[43] 18 U.S.C. § 208(b)(1), (b)(3).

[44] FFDCA § 712(c)(2).

[45] FFDCA § 712(b)(2).

[46] 18 U.S.C. § 208(a).

[47] 18 U.S.C. § 208(a).

[48] 18 U.S.C. § 208(b)(1).

[49] 18 U.S.C. § 208(b)(3).

[50] FFDCA § 712(c)(2)(A).

retains the right to grant a waiver to any member of such advisory panel to participate in "a particular matter considered in a committee meeting," either as a voting or non-voting member of the advisory committee, when the Secretary determines that "it is necessary to afford the advisory committee essential expertise."[51]

Provisions in S. 3187 and H.R. 5651 regarding advisory committee conflicts of interest are summarized and compared with current law and with each other in **Table 13**.

Table 13. Advisory Committee Conflicts of Interest

Current Law (FFDCA Sec. 712)	S. 3187 (as passed) Title XI	H.R. 5651 (as passed)
Recruitment		
The Secretary must develop and implement strategies on effective outreach to potential members of advisory committees in the academic community, professional and medical societies, and patient and consumer groups, with input to determine the most effective informational and recruitment activities.	Would make technical drafting changes to the current law and add language to the recruitment requirements for potential advisory committee appointees to require the Secretary to develop and implement strategies on increasing the number of special government employees across medical and scientific specialties in areas where the Secretary would benefit from specific scientific, medical, or technical expertise necessary for the performance of regulatory responsibilities. [Sec. 1121]	Contains similar technical drafting changes and recruitment language to that in S. 3187, but would not add the language on strategies to increase the number of special government employees. [Sec. 602]
	Would add a new provision on recruitment through referrals that would require the Secretary to request, at least every 180 days, referrals from stakeholders such as the Institute of Medicine, the National Institutes of Health, product developers, patient groups, disease advocacy organizations, professional societies, medical societies such as the American Academy of Medical Colleges, and other governmental organizations. Such recruitment through referrals would further the goal of including on the committees highly qualified and specialized experts in the specific diseases to be considered by the committees. [Sec. 1121]	Also would add a new provision requiring the Secretary to request, at least every 180 days, referrals for potential advisory committee members from some of the same stakeholders as listed in S. 3187. Does not explicitly include the Institute of Medicine, the National Institutes of Health, or the American Academy of Medical Colleges in its list of stakeholders, but does include academic organizations, professional societies, medical societies, and governmental organizations. Does not specify that these recruitments through referrals would be "to further the goal of including in advisory committees highly qualified and specialized experts in the specific diseases to be considered by such advisory committees," as in S. 3187. [Sec. 602]
In conducting advisory committee recruitment activities, the Secretary must take into account the committees with the greatest number of	Would not change current law.	Would require the Secretary to also take into account the levels of activity, including the number of annual meetings, as well as the numbers of vacancies of the advisory committees. [Sec. 602]

[51] FFDCA § 712(c)(2)(B).

Current Law (FFDCA Sec. 712)	S. 3187 (as passed) Title XI	H.R. 5651 (as passed)
vacancies.		
Recruitment activities may include advertising, making contact information widely available, and developing a method through which entities receiving funding from certain government agencies can identify a person the FDA can contact on the nomination of individuals to advisory committees.	Would not change current law.	Same as current law, but would add a provision that the Secretary must seek to ensure that she has access to the most current expert advice. [Sec. 602]
Potential conflicts of interest and waivers		
When considering an appointment to an advisory committee, the Secretary shall review an individual's expertise and financial disclosure report. Prior to an advisory committee meeting regarding a "particular matter" (as that term is used in 18 USC 208), each committee member who is a full-time government employee or special government employee must disclose to the Secretary any financial interests in accordance with 18 USC 208. With some exceptions, members may not participate with respect to a particular matter if they have, or an immediate family member has, a financial interest that could be affected, although the Secretary may waive this prohibition if the Secretary "determines it necessary to afford the advisory committee essential expertise."	Would change the criteria that the Secretary must consider in making an appointment to an FDA advisory committee. The Secretary would no longer be required to review, for potential advisory committee appointees, an individual's expertise and financial disclosure report "so as to reduce the likelihood that an appointed individual will later require" a written determination, certification, or waiver for a potential conflict of interest in order to serve at an advisory committee meeting. [Sec. 1121] Would retain the FDA's current prohibition regarding conflicts of interest and associated waiver for essential expertise. Would require the Secretary to consider, when granting such a waiver, the type, nature, and magnitude of the financial interest that could constitute a potential conflict of interest, as well as the public health interest in having the member's expertise. [Sec. 1121]	Also would change the criteria that the Secretary must consider in making an appointment to an advisory committee and eliminate the review requirement. [Sec. 602] Would retain the FDA's current prohibition regarding conflicts of interest and associated waiver for essential expertise, as well as the requirements to disclose such waivers (either 15 or more days in advance, or less than 30 days in advance but before the meeting, depending on when the financial interest becomes known) before an advisory committee meeting. Written determinations and written certifications would still be required to be disclosed on the FDA website, as under current law, but this section would add that the Secretary's reasons for the determination or certification could include the public health interest in having the member's expertise with respect to the particular matter before the committee. [Sec. 602]
Limitation on number of exceptions		
The FDA Amendments Act of 2007 (FDAAA) limited the number of exceptions (such as waivers under the provisions of the criminal financial conflict of interest statute) for FY2008-2012. [P.L. 110-85, Sec. 701;	Would strike the provision that limited the number of exceptions (such as waivers under the provisions of the criminal financial conflict of interest statute) the Secretary could grant in FY2008 through FY2012. [Sec 1121]	Also would strike the provision limiting the number of exceptions (such as waivers under the provisions of the criminal financial conflict of interest statute) the Secretary could grant in FY2008 through FY2012. [Sec. 602]

Current Law (FFDCA Sec. 712)	S. 3187 (as passed) Title XI	H.R. 5651 (as passed)
FFDCA 712(c)(2)(c)]		
Reports		
The Secretary must submit to certain congressional committees annual reports that describe certain information regarding vacancies, nominees, and disclosures required. For example, current law requires a report of the aggregate number of disclosures required of written determinations, written certifications, and waivers, that are included in the public record and transcript of each advisory committee meeting.	Would require the Secretary to make these annual reports publicly available, but would not otherwise alter current reporting requirements. [Sec. 1121]	Would change the types of information that the Secretary is required to submit in an annual report to certain congressional committees. Would eliminate descriptions of certain information in these reports. In addition to reporting the number of vacancies on each advisory committee, as required in current law, would require a report on the number of persons nominated for participation at meetings for each advisory committee, the number of persons so nominated and willing to serve, and the number of persons contacted for service as members who did not participate because of the potential for such participation to constitute a disqualifying financial interest under 18 USC 208, as well as those who did not participate for other reasons. [Sec. 602] Would require the Secretary to report the number of members attending meetings for each advisory committee. [Sec. 602] Would require a report of the aggregate number of disclosures that are included in the public record and transcript of each advisory committee meeting, and the percentage of individuals to whom such disclosures did not apply who served on the committee. [Sec. 602] Like S. 3187, also would require the Secretary to make the annual reports publicly available, but the Secretary would have 30 days after submitting the report to the specified committees to do so. [Sec. 602]
Guidance		
The Secretary must review, and update as necessary, guidance regarding conflict of interest waiver determinations with respect to advisory committees at least once every 5 years.	Would require the Secretary to issue guidance describing her review of the financial interests and involvement of advisory committee members that are reported under the provision on disclosure prior to a meeting involving a "particular matter" (as defined in 18 USC 208) by a member who is either a full-time or special government employee, but that the Secretary finds do not meet the definition of a disqualifying interest under 18 USC 208 for purposes of participating	Would require the Secretary to review guidance with respect to advisory committees regarding disclosure of conflicts of interest and the application of 18 USC 208. Also would require the Secretary to update the guidance to ensure the FDA receives appropriate access to needed scientific expertise, with due consideration to requirements under 18 USC 208. [Sec. 602]

Current Law (FFDCA Sec. 712)	S. 3187 (as passed) Title XI	H.R. 5651 (as passed)
	in the particular matter. [Sec. 1121]	
Applicability		
Current law.	No provision.	Amendments made by this section would apply starting October 1, 2012. [Sec. 602]

Source: CRS analysis of current law, S. 3187 (as passed), and H.R. 5651 (as passed).

Administrative Reforms and Miscellaneous Topics[52]

A number of additional provisions in the two bills are summarized and compared in **Table 14**. These provisions are:

- Reauthorization of the Critical Path Public-Private Partnerships;
- Guidance regarding Internet promotion of medical products;
- Electronic submission of applications;
- Tanning bed labeling;
- Global clinical trials;
- Regulatory science;
- Information technology;
- Reporting requirements for medical products covered by user fee agreements;
- Strategic integrated management plan for FDA workforce;
- Patient participation in medical product discussions;
- Nanomaterials in FDA-regulated products;
- GAO report regarding online pharmacies;
- Medication and device errors;
- Statutory Pay-As-You-Go statement;
- Communicating drug information, including to underrepresented subgroups;
- Report on small businesses;
- Whistleblower protection, U.S. Public Health Service;
- Clinical trial registration;
- Compliance date for over-the-counter sunscreen products;

[52] Many members the team contributed to this section of the report. For follow-up discussions, contact Susan Thaul, Specialist in Drug Safety and Effectiveness.

- Changes to the Controlled Substances Act (CSA); and
- Prescription drug monitoring programs.

Table 14. Administrative Reforms and Miscellaneous Provisions

Current Law	S. 3187 (as passed)	H.R. 5651 (as passed)
Critical Path Public-Private Partnerships; reauthorization		
The Secretary may enter into agreements (Critical Path Public-Private Partnerships) with educational or tax-exempt organizations to implement research, education, and outreach projects regarding medical products, in order to foster innovation, accelerate product development, and enhance product safety. Current law authorizes the appropriation of $5 million for FY2008 and such sums as may be necessary for each of FY2009-FY2012. [FFDCA 566; 21 USC 360bbb-5]	Would reauthorize the Critical Path Public-Private Partnerships, authorizing the appropriation of *such sums as may be necessary* through FY2017. [Sec. 1102]	Also would reauthorize the Critical Path Public-Private Partnerships, authorizing the appropriation of *$6 million for each* of FY2013 through FY2017. [Sec. 851]
Guidance re: Internet promotion of medical products		
No provision.	Would require the Secretary, within 2 years of enactment, to issue a guidance document that describes FDA policy regarding the promotion of FDA-regulated medical products using the Internet (including social media). [Sec. 1122]	No provision.
Electronic submission of applications		
No provision.	Would require the Secretary to issue, after notice and comment, guidance on how to electronically submit new drug applications, investigational new drug applications (but not emergency investigational new drug applications), abbreviated new drug applications, biologics license applications, and applications for licensure of interchangeable or biosimilar products. These listed submissions would have to be submitted in the specified electronic format no earlier than 24 months after the final guidance is issued. Provides that the Secretary may create a timetable for further standards for electronic submission and set forth criteria for waivers and exemptions from the electronic submission requirements. Would require certain pre-submissions, submissions, and supplements to pre-submissions or submissions	Identical to S. 3187, Sec. 1123. [Sec. 603]

Current Law	S. 3187 (as passed)	H.R. 5651 (as passed)
	related to devices to include an electronic copy, after the Secretary issues final guidance. [Sec. 1123]	
Tanning bed labeling		
No provision.	Would require the Secretary to determine within 18 months of enactment whether to amend the warning label requirements for sunlamps to include specific requirements to more clearly and effectively convey the risks of developing irreversible damage to the eyes and skin, including skin cancer. [Sec. 1125]	No provision.
Global clinical trials		
No provision.	Would require the Secretary to work with other regulatory authorities, medical research companies, and international organizations to harmonize global clinical trial standards for medical products, in order to (1) enhance medical product development; (2) facilitate the use of foreign data; and (3) reduce duplicative studies. Would not alter the current standards for premarket review of medical products. Also would require the Secretary, in deciding whether to approve, license, or clear a drug or device, to accept data from clinical trials outside the United States, as long as such data meet applicable standards. The Secretary would be required to provide a sponsor with a written explanation in the event that such data were found to be inadequate. [Sec. 1126]	No provision.
Regulatory science		
No provision.	Would require the Secretary, within 1 year of enactment, to establish a strategy and implementation plan, consistent with user fee program performance goals, for advancing regulatory science. Such plan must identify a vision and priorities related to medical product decision-making, and ways to address regulatory and scientific gaps, among other stated requirements. Would require the Secretary to submit to Congress annual performance reports on these goals for FY2013-2017, and GAO to report, by	Although regulatory science requirements or metrics are mentioned in some user fee reauthorizations, there is no provision addressing a strategic approach for any or all medical products.

Current Law	S. 3187 (as passed)	H.R. 5651 (as passed)
	January 1, 2016, on the FDA's progress toward these goals. [Sec. 1127]	
Information technology		
No provision.	Would require the Secretary, within 1 year of enactment, to report on the development and implementation of a plan to modernize FDA's information technology systems and align them with the strategic goals of the agency, consistent with existing GAO recommendations (i.e., GAO-12-346, March 15, 2012). Would require GAO to report, by January 1, 2016, on the FDA's progress to meet the goals set out in such plan. [Sec. 1128]	No provision.
Reporting requirements for medical products covered by user fee agreements		
Existing user fee authorities for new drugs include annual performance and fiscal reporting requirements. [FFDCA 736B; 21 USC 379h–2]	Would create a new FFDCA Sec. 715, "Reporting Requirements," to expand annual reporting requirements for drugs and biological products covered by user fee agreements for FY2013-FY2017, in addition to requirements proposed in Titles I-IV of the bill regarding reauthorization of the existing prescription drug user fee program, and the proposed generic drug and biosimilar biologics user fee programs. The Secretary would be required to report to Congress, within 120 days of the end of each fiscal year, on a number of stated matters regarding all applications for approval of new drugs or biologics filed in the prior fiscal year. Such matters would include the percentage of applications approved, or not approved for various reasons, the number of applications that met goals specified in the FDA-industry agreements to which the user fee authorizations refer, average time to decision, and specified statistics on intermediate steps in the application review process. Reports would be required in the same manner for generic drug applications, and for biosimilar biologics, also to include stated information for each. [Sec. 1129]	No provision; i.e., no additional reporting requirements in addition to those proposed in Titles I-IV of the bill regarding reauthorization of the existing prescription drug user fee program, and proposed generic drug and biosimilar biologics user fee programs.
Strategic integrated management plan for FDA workforce		
No provision.	Would require the Secretary, within 1 year of enactment, to submit an	No provision.

Current Law	S. 3187 (as passed)	H.R. 5651 (as passed)
	integrated management strategy to Congress. The plan must identify goals and priorities for CDER, CBER and CDRH,[a] describe the actions FDA will take to develop the workforce at these centers, and establish performance measures. GAO would be required, by January 1, 2016, to report, among other specified matters, on the effectiveness of these actions toward achieving the goals and priorities in the report. [Sec. 1130]	
Patient participation in medical product discussions		
No provision.	Would require the Secretary to develop and implement strategies to solicit patients' views during the medical product development and regulatory processes, including the inclusion of a patient representative in agency meetings who has minimal or no financial interest in the medical products industry. [Sec. 1132]	No provision.
Nanomaterials in FDA-regulated products		
No provision.	Would require the Secretary, within 180 days of enactment, to establish within FDA a Nanotechnology Regulatory Science Program to enhance the scientific knowledge regarding nanomaterials included or intended for inclusion in products regulated under the FFDCA, to address: (1) the potential toxicology of such materials; (2) the effects of such materials on biological systems; and (3) the interaction of such materials with biological systems. The section states program purposes, addresses administrative matters, and would require a report on the program (to be posted on the FDA website) by March 15, 2015. The program would take effect on October 1, 2012 or upon enactment (whichever is later), and would sunset October 1, 2017. [Sec. 1133]	No provision.
Online pharmacies; GAO report		
No provision.	Would require GAO, within 1 year of enactment, to report on a number of specified problems posed by online pharmacy websites that violate state or federal law. [Sec. 1134]	No provision.

Current Law	S. 3187 (as passed)	H.R. 5651 (as passed)
Medication and device errors		
No provision.	Would require the Secretary to continue and further coordinate HHS activities related to the prevention of medication and device errors, including those errors that affect the pediatric patient population. [Sec. 1135]	No provision.
Statutory Pay-As-You-Go-Act of 2010 (PAYGO) procedure		
Under the Statutory Pay-As-You-Go (PAYGO) Act of 2010 (Title I of P.L. 111-139), the 5- and 10-year budgetary effects of direct spending and revenue legislation enacted during a session are placed on respective scorecards. At the end of a session of Congress, if either scorecard shows an increase in the deficit, a sequestration of non-exempt budgetary resources is required to eliminate such deficit. Under the law, the budgetary effects of legislation are determined by either a statement in the Congressional Record submitted by the chair of the House or Senate Budget Committee, as referenced in the legislation, or by the Office of Management and Budget (OMB).[b]	Would provide that the budgetary effects of this bill, for purposes of the Statutory PAYGO Act, are determined by the statement submitted to be printed in the Congressional Record by the chair of the Senate Budget Committee, provided that such statement is submitted prior to the vote on passage. [Sec. 1136]	No provision.
Communicating drug information, including to underrepresented subgroups		
No provision.	Would require the Secretary to review FDA's communication plan to inform and educate providers, patients, and payors about the benefits and risks of medical products; and post the plan, modified if necessary, within one year of enactment on the FDA Office of Minority Health website. Taking into account the goals and principles in the HHS Strategic Action Plan to Reduce Racial and Ethnic Disparities; the nature of the medical product, available health and disease information, and means of communicating information, the modified plan must address a strategy and a process for implementing improvements. [Sec. 1137]	No provision.

Current Law	S. 3187 (as passed)	H.R. 5651 (as passed)
Report on small businesses		
No provision.	Would require the Commissioner of Food and Drugs to submit a report to Congress within one year of enactment with specified details regarding FDA interactions with small businesses, barriers encountered, and recommendations for changes in the user fee structure. [Sec. 1138]	No provision.
Whistleblower protection for the Commissioned Corps of the U.S. Public Health Service		
PHSA Sec. 221(a) lists the rights, benefits, privileges, and immunities of commissioned officers in the U.S. Public Health Service (USPHS) by reference to the rights, benefits, privileges, and immunities of commissioned officers in the Army, as provided in USC Title 10.	Would add to the existing list the provision at 10 USC 1034, which would prohibit any restriction on lawful communication by a USPHS Commissioned Officer with a Member of Congress or the HHS Inspector General (a so-called "whistleblower" protection). [Sec. 1139]	No provision.
Clinical trial registration: regulations and GAO report		
The Secretary must maintain and operate a data bank of specified information on applicable clinical trials. FDAAA expanded the scope, which now includes, for example, study design and recruitment contacts, and results. FDAAA also required the Secretary to issue regulations. [PHSA 402(j); 42 USC 282(j)]	Would require the Secretary, acting through the NIH Director, to issue a notice of proposed rulemaking (within 180 days of enactment) and final regulations (within 180 days of the notice) "on the registration of applicable clinical trials by responsible parties," or to submit a letter to Congress with reasons for the delay. Would require, within 2 years of the final rule's issuance, a GAO report, to include (1) specified content, on the implementation of the registration and reporting requirements of applicable drug and device clinical trials, and (2) recommendations for administrative or legislative actions to increase the compliance with the requirements of PHSA 402(j). [Sec. 1140]	No provision.
Compliance date for over-the-counter sunscreen products		
The FDA Modernization Act of 1997 (P.L. 105-115) required the Secretary to issue regulations re: sunscreen labeling, effectiveness testing, and other specified regulatory matters, within 18 months of its enactment in November, 1997. After several interim steps, FDA published a final rule re: labeling and effectiveness testing on June 17, 2011, and amended the rule on May 11, 2012	Would establish compliance dates as per the May 11, 2012 amendment to the final rule. [Sec. 1142] (Note: If enacted, this provision would prevent any subsequent delays in the compliance dates.)	No provision.

Current Law	S. 3187 (as passed)	H.R. 5651 (as passed)
to delay the stated compliance dates for 6 months, such that: products with annual sales less than $25,000 must comply by December 17, 2013; and all other products subject to the rule must comply by December 17, 2012. [77 *Federal Register* 27591]		
Changes to the Controlled Substances Act (CSA)		
The Controlled Substances Act (CSA) establishes five schedules for controlled substances (including drugs) based upon each substance's medical use, potential for abuse, and safety or dependence liability. Schedule I is the most restrictive, schedule V the least restrictive. The CSA further provides a mechanism for substances to be added to a schedule, removed from a schedule, or transferred from one schedule to another. [21 USC 801 et seq.]	Would add specified synthetic drugs, including those that mimic the effects of cannabis or marijuana, to schedule I under the CSA. [Sec. 1152]	No provision.
The CSA allows the Attorney General to place a substance on schedule I temporarily to avoid imminent hazards to public safety. Temporary scheduling expires at the end of 1 year, with a possible 6-month extension. [21 USC 811(h)]	Would extend the initial period of temporary scheduling from 1 year to 2 years and the extension from 6 months to 1 year. [Sec. 1153]	No provision.
The CSA establishes penalties for unlawfully manufacturing, distributing, or dispensing controlled substances, or possessing controlled substances with intent to manufacture, distribute, or dispense them. [21 USC 841(b), 21 USC 841(c)]	The specified synthetic drugs added to schedule I would not be subject to any mandatory minimum prison sentences otherwise required to be imposed under the CSA. [Sec. 1154]	No provision.
Unless otherwise specified, hydrocodone in all doses and combinations is on schedule II, but certain specified doses and combinations are on schedule III. [21 USC 812]	Would strike from current law language placing specific doses and combinations of dihydrocodeinone (i.e., hydrocodone) on schedule III, which would have the effect of placing them on schedule II (and therefore requiring a new prescription, rather than a refill, for each dispensing). Would also add language to keep these drugs subject to penalties applicable to most schedule III drugs. [Sec. 1141]	No provision.
Prescription drug monitoring programs: recommendations on interoperability standards		
State prescription drug monitoring programs (PDMPs) may receive support from two federal grant programs: one operated by HHS (not currently funded) [42 USC 280g-3] and one operated by DOJ	Would allow the Secretary and the Attorney General to develop recommendations on PDMP interoperability standards for the exchange of PDMP information by states receiving grants under two	No provision.

Current Law	S. 3187 (as passed)	H.R. 5651 (as passed)
(currently funded) [established in appropriations, P.L. 107-77, H.Rept. 107-278].	federal programs. Would specify topics to be considered in the development of recommendations. Would require the Attorney General to submit a report on enhancing state PDMP interoperability, to include specified components. [Sec. 1143]	

Source: CRS analysis of current law, S. 3187 (as passed), and H.R. 5651 (as passed).

Notes: Italics are used to emphasize differences between bills.

a. This refers to three FDA centers, the Center for Drug Evaluation and Research, the Center for Biologics Evaluation and Research, and the Center for Devices and Radiological Health.

b. For more information on PAYGO procedures, see CRS Report R41157, *The Statutory Pay-As-You-Go Act of 2010: Summary and Legislative History*, by Bill Heniff Jr.

Next Steps

The Senate voted 96-1 to pass S. 3187 on May 24, 2012. The House voted 387-5 to pass H.R. 5651 on May 30, 2012. PDUFA and MDUFA sunset on October 1, 2012 and committee bipartisan leadership has been committed to completing the reauthorizations before FDA would have to initiate lay-off notification procedures that would disrupt drug and device application review and postmarket safety activities. FDA-focused newsletters and the national media report that "ping-pong" negotiations, rather than a formal conference committee, are underway between House and Senate staff and Members to resolve the differences between the bills.[53]

Despite a successful bipartisan effort to build a core set of drug and device provisions that could join, but not derail, must-pass user fee provisions, there remain complex issues that Members of Congress will likely pursue after a final bill is passed out of S. 3187 and H.R. 5651. These include changing the premarket approval and clearance procedures for medical devices, further developing a supply chain system that meets global demands, and looking at whether federal health program drug payment policies influence drug shortages. Whether Congress needs a must-pass vehicle, next facing FDA in 2017, to achieve these legislative changes remains to be seen.

[53] "PDUFA Clears House, Awaits Reconciliation With Senate Version," Drug Industry Daily, vol. 11, no. 107, May 31, 2012.

Appendix. Acronyms

510(k)	premarket notification (refers to FFDCA Sec. 510(k))
AG	Attorney General
ANDA	abbreviated new drug application
API	active pharmaceutical ingredient
BPCA	Best Pharmaceuticals for Children Act
BPCIA	Biologics Price Competition and Innovation Act of 2009
BSUFA	Biosimilar User Fee Act of 2012
CBER	Center for Biologics Evaluation and Research
CBP	Customs and Border Protection
CDC	Centers for Disease Control and Prevention
CDER	Center for Drug Evaluation and Research
CDRH	Center for Devices and Radiological Health
CFR	Code of Federal Regulations
CGMP	current good manufacturing practice
CPI	Consumer Price Index
CSA	Controlled Substances Act (21 USC 801 et seq.)
DEA	Drug Enforcement Administration
DMF	drug master file
DOJ	Department of Justice
E&C	House Committee on Energy and Commerce
ETASU	elements to assure safe use
FACA	Federal Advisory Committee Act
FDA	Food and Drug Administration
FDAAA	FDA Amendments Act of 2007
FDAMA	FDA Modernization Act of 1997
FFDCA	Federal Food, Drug, and Cosmetic Act (21 USC 301 et seq.)
FNIH	Foundation for the NIH
FOIA	Freedom of Information Act
FTC	Federal Trade Commission
FTE	full time equivalent position
GAIN	Generating Antibiotic Incentives Now Act
GAO	Government Accountability Office (formerly General Accounting Office)
GDUFA	Generic Drug User Fee Amendments of 2012
HDE	humanitarian device exemption
HELP	Senate Committee on Health, Education, Labor, and Pensions
HHS	Department of Health and Human Services
HIT	health information technology

IDE	investigational device exemption
IND	investigational new drug
LDT	laboratory-developed test
MDA	Medical Device Amendments Act of 1976
MDTCA	Medical Device Technical Corrections Act of 2004
MDUFA	Medical Device User Fee Amendments of 2007 or 2012
MDUFMA	Medical Device User Fee and Modernization Act of 2002
MDUFSA	Medical Device User Fee Stabilization Act of 2005
NDA	new drug application
NIH	National Institutes of Health
NSE	non-substantial equivalence
ODAC	Oncologic Drug Advisory Committee
OMB	Office of Management and Budget
PAC	Pediatric Advisory Committee
PAS	prior approval supplement
PAYGO	Pay-As-You-Go Act of 2010
PDMP	prescription drug monitoring program
PDUFA	Prescription Drug User Fee Act (or Amendments)
PeRC	Pediatric Review Committee
PET	positron emission tomography
PHSA	Public Health Service Act (42 USC Chapter 6A)
PL	Public Law
PMA	premarket approval
PMDSIA	Pediatric Medical Device Safety and Improvement Act
PREA	Pediatric Research Equity Act
QIDP	qualified infectious disease product
QP	qualifying pathogen
REMS	Risk Evaluation and Mitigation Strategies
RxTEC	Pharmaceutical Traceability Enhancement Code
USC	United States Code

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