



FDA Legislation in the 110th Congress: A Guide to S. 1082 and H.R. 2900

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Summary

Both the House and the Senate have passed comprehensive legislation to reauthorize existing Food and Drug Administration (FDA) programs and expand the agency's authority to ensure the safety of prescription drugs, medical devices, and biologics. The Senate passed the Food and Drug Administration Revitalization Act (S. 1082) on May 9, 2007. The House passed the Food and Drug Administration Amendments Act of 2007 (H.R. 2900) on July 11, 2007.

At its core, the legislation renews authority for two key user fee programs that are set to expire on October 1, 2007: the Prescription Drug User Fee Act (PDUFA; P.L. 107-188) and the Medical Device User Fee and Modernization Act (MDUFMA; P.L. 107-250). These account for 87% of FDA's user fee revenue, and 19% of FDA's total FY2008 program level budget. Without the reauthorizations, and absent a substantial increase in FDA's annual appropriations, the agency would lose a significant source of funding. FDA had warned that a failure to reauthorize the user fee programs before August 1, 2007, would require the agency to issue layoff notices, but the agency has reportedly forestalled that necessity by switching to reserve funds.

In addition to user fee programs, the bills reauthorize two other FDA authorities related to prescription drugs for pediatric populations, which are also due to expire on October 1, 2007: the Best Pharmaceuticals for Children Act (BPCA; P.L. 107-109) and the Pediatric Research Equity Act (PREA; P.L. 108-155). These laws provide marketing exclusivity incentives and requirements for studying pediatric use of *on-patent* and *off-patent* drugs. S. 1082 and H.R. 2900 also contain provisions related to drug safety, pediatric medical devices, clinical trial registration, and the creation of a new nonprofit entity to assist FDA with its mission. The bills' overlapping provisions are similar, but not identical.

S. 1082 contains some additional provisions that are not present in H.R. 2900, on the topics of food safety, prescription drug importation, and domestic pet turtle market access. Attempts to expand the legislation to address several other FDA-related issues, for example, follow-on biologics and genetic testing, have thus far been unsuccessful. Differences between the bills may be addressed in conference.

This report contains background information about the FDA relevant to S. 1082 and H.R. 2900. It presents a comparative overview of the bills' contents, and contains links to pertinent CRS reports. This report will be updated as further legislative events warrant.

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Introduction

Both chambers of Congress have passed comprehensive legislation to reauthorize expiring programs at the Food and Drug Administration (FDA), and to expand the agency's authority to help ensure the safety of certain medical products. The bills are the Food and Drug Administration Revitalization Act (S. 1082), and the Food and Drug Administration Amendments Act of 2007 (H.R. 2900). S. 1082 and H.R. 2900 represent the most comprehensive FDA legislation since the Food and Drug Administration Modernization Act of 1997 (FDAMA; P.L. 105-115).

The primary driver of the legislation is the renewal of FDA's authority for two key user fee programs set to expire at the end of FY2007: the Prescription Drug User Fee Act (PDUFA; P.L. 107-188), and the Medical Device User Fee and Modernization Act (MDUFMA; P.L. 107-250). FDA had reportedly urged Congress to complete its reauthorization efforts before August 1, 2007 (rather than by the program's termination date of October 1, 2007), because of a requirement that FDA notify employees at least 60 days in advance of layoffs, which would be necessary without PDUFA and MDUFMA funds.¹ The media report that FDA has switched to reserve funds to forestall the issuance of layoff notifications, the effect of which is a hiring freeze at FDA.² In addition, the FDA Commissioner has reportedly stressed that the funding uncertainty is harming the morale of employees: 30% of whom are at a point where they can retire.

The bills also would reauthorize two other expiring authorities, which are related to pediatric pharmaceuticals: the Best Pharmaceuticals for Children Act (BPCA; P.L. 105-115; reauthorized in P.L. 107-109), and the Pediatric Research Equity Act (PREA; P.L. 108-155). In addition, the bills address a number of other issues of concern to Congress and to the public.

The FDA, an agency within the Department of Health and Human Services (HHS), regulates the *safety* of most human foods,³ all animal feeds, and certain other products such as cosmetics. The agency also regulates the *safety and effectiveness* of human drugs, biologics (e.g., vaccines), medical devices, and animal drugs.⁴ Those products regulated for effectiveness must be reviewed and approved by FDA before they can be placed in commerce, a process called *premarket approval*. (FDA is tasked with postmarket surveillance for these products as well.) Products regulated only for safety may enter commerce with little FDA oversight, though the agency may inspect production facilities and require that certain good manufacturing practices be carried out. FDA has the statutory authority to withdraw from commerce any product it regulates that it determines to be unsafe.

Media coverage of issues related to the safety of food (e.g., spinach), drugs (e.g., Vioxx), and medical devices (e.g., cardiac stents) have brought congressional attention to FDA's performance and the funding it has available to carry out its statutory responsibilities. For those products requiring premarket approval, a central issue for the 110th Congress is how best to balance the need for the agency to help speed the products it regulates to market if they are safe and effective, and correct them or keep or remove them from the market if they are not. For human foods,

¹ Joe Reichard, "FDA Running on Budgetary Fumes, Chief Says" *CQ Healthbeat News*, August 2, 2007, 4:40 p.m.

² Anna Edney, "FDA To Avoid Layoff Notices By Dipping Into Reserves," *Congress Daily, Health*, August 2, 2007.

³ The United States Department of Agriculture (USDA) regulates the safety of meat and poultry products.

⁴ Regulation of biologics for animal use is overseen by the USDA.

animal feeds, and other products not requiring premarket approval, key issues relate to FDA's ability to assure product safety and protect public health by preventing health threats from occurring, or by identifying and responding to problems quickly.

Drug and Device User Fees

In order to bring revenue into FDA to help speed products to market, Congress has passed several measures authorizing FDA to collect user fees from the products' manufacturers. Some have questioned whether the agency's reliance on fees it collects from the companies that it regulates is appropriate, calling instead for greatly increased appropriations for the agency. Nevertheless, efforts to reauthorize the two expiring user fee authorities (PDUFA and MDUFMA) are already underway.

Income from PDUFA and MDUFMA represents, by far, the largest proportion of FDA's user fee revenue, and a significant proportion of the agency's overall budget. According to FDA's FY2008 budget request, PDUFA will generate \$339,195,000, and MDUFMA will generate \$47,500,000. Combined, these fees would account for 87% of FDA's user fee revenue, and 19% of its total program level budget in FY2008.

PDUFA was first enacted in 1992 (P.L. 102-571), and has been reauthorized twice; once by the Food and Drug Administration Modernization Act of 1997 (FDAMA, P.L. 105-115), and a second time by the Public Health Security and Bioterrorism Preparedness and Response Act of 2002 (P.L. 107-188). PDUFA authorizes the FDA to collect fees from companies that produce certain human drugs and biological products, and to use the revenue for the review of new product applications. PDUFA also incorporates, by reference, performance goals aimed primarily at reducing FDA premarket review times.

MDUFMA, first enacted in 2002, established user fees for FDA's review of medical device applications. Like PDUFA, MDUFMA incorporated, by reference, performance goals for many types of premarket device reviews. MDUFMA also allowed third-parties to conduct establishment inspections, and added new regulatory requirements for reprocessed single-use devices. The expiring authorities within MDUFMA are those related to user fees and the associated performance goals.

Pediatric Drug Research

In part to protect children from the risks of participating in clinical trials, researchers did not often test drugs on that population. As a result, information about appropriate dosage levels for and potential side effects of "adult" medications in children were unknown, frequently leaving clinicians with pediatric patients the choice of prescribing nothing, or something with an unknown effect. In 1997, Congress gave FDA a tool, in BPCA, to encourage pediatric drug research—extended marketing exclusivity in exchange for trials investigating a drug's effect on pediatric populations. Meanwhile, FDA's attempts to require, as part of new drug applications, assessments of how new drugs would affect pediatric populations were stopped by the courts until Congress, in 2003, codified that requirement in PREA. BPCA and PREA provide marketing exclusivity incentives and requirements for studying pediatric use of both *on-* and *off-patent* drugs.

Other FDA Issues

The following topics are addressed in one or both reauthorization bills.

Pediatric Medical Devices

It has been reported that developing medical devices for children is less profitable and more problematic than developing them for adults. This is because fewer children need medical devices than adults, and because children have physical attributes (e.g., size, biochemistry, growth rates), activities, and environmental influences that vary from those of adults. The result has been characterized as a critical need for pediatric medical devices that help diagnose and treat diseases and conditions affecting children. Both S. 1082 and H.R. 2900 contain provisions offering incentives to manufacturers to create pediatric medical devices, and giving FDA the authority to require postmarket studies of approved pediatric devices to ensure their continued efficacy and safety.

Drug Safety

While premarket clinical trials reveal many of the adverse effects of medical products, others may not become apparent until a product is on the market. This may be because the adverse effects require a period of years or decades to manifest, or it may be because the adverse effects are so rare that they require use by a large number of people for them to be recognized as drug-related. In some instances, only a small proportion of people who will take the drug are susceptible to a specific effect, requiring a large swath of the population to use a drug before the adverse effect is seen. S. 1082 and H.R. 2900 include provisions focused on buttressing FDA's system for collecting data on marketed products, sifting through the massive amounts of information to identify situations that merit FDA action, and providing new authorities to allow FDA to require manufacturers to take some actions.

Clinical Trials Databases

Medical journals tend only to publish the results of clinical trials demonstrating a product's effectiveness, as negative studies do not draw readers in the same way. Product manufacturers may be reluctant to make unsuccessful results public as well, to avoid both alerting potential customers to problems and informing competitors of their activities. However, in 2004, Congress and others raised questions about the safety and effectiveness of several FDA-approved biomedical products about which negative trial results had not been publicly disclosed (e.g., antidepressants, cardiac stents).⁵ The issue of public access to negative trial results then gained significant traction. Both S. 1082 and H.R. 2900 contain provisions relating to the public registration of clinical trials and the public posting of their results.

⁵ Shankar Vedantam, "Antidepressant Makers Withhold Data on Children," *Washington Post*, January 29, 2004, p. A1; and Catherine De Angelis et al., "Clinical Trial Registration: A Statement from the International Committee of Medical Journal Editors," *New England Journal of Medicine*, vol. 351, no. 12, September 16, 2004, p. 1250.

Conflicts of Interest

FDA uses advisory committees to provide the agency with independent advice from outside experts on issues related to human and veterinary drugs, biological products, medical devices, and food. Advisory committees make recommendations to FDA, which FDA may or may not follow. To be credible and useful, many say that committees need to be free from or reduce conflicts of interest. However, others note that the most expert members in the field are often those involved directly or indirectly in the activities about which FDA is seeking advice, creating the potential for such conflicts. In 2006 and 2007, the media has reported that FDA advisory committees are biased in favor of drug approval, and that many committee members have conflicts of interest.⁶ Both S. 1082 and H.R. 2900 contain provisions that would revise FDA's approach to advisory committee members' conflicts of interest.

Reagan-Udall Foundation

The year 2000 marked the start of a slowdown in new drug and biologic submissions to regulatory agencies worldwide. In 2004, puzzled over why, despite advances in biomedical sciences, there had been a disappointing decline in innovative medical products submitted for approval, FDA investigated this issue. Its report noted the rising difficulty and unpredictability of medical product development and called for a concerted effort to modernize the scientific tools (e.g., in vitro tests, computer models, qualified biomarkers, and innovative study designs) and harness the potential of bioinformation used to evaluate and predict safety, effectiveness, and manufacturability of candidate medical products.⁷ S. 1082 and H.R. 2900 propose the creation of a Reagan-Udall Foundation, a nonprofit corporation that would support FDA in those tasks.

Importation of Prescription Drugs

The high cost of prescription drugs in the United States has prompted some consumers to seek medications from foreign sources. Current law permits only the manufacturer of a prescription drug to import it. Such importation is tightly regulated by FDA based on law. Because imports acquired outside of this regulated chain-of-custody may come from foreign sources not subject to the same rigorous safety and inspection requirements that FDA-regulated manufacturers and importers face, the law prohibits all other drug importation.

Some lawmakers have tried to find ways to allow access to lower priced medications—perhaps enabling individuals or commercial importers to purchase medications from foreign sources—while still ensuring the products' safety. One title of S. 1082 was written to allow and regulate some importation of prescription drugs. An amendment to require the Secretary of HHS (hereinafter referred to as the Secretary) to certify that the program would be safe and cost-effective effectively nullifies the detailed drug importation language.

⁶ See, for example, Shankar Vedantam, "Group Says FDA, Advisory Panels Show Bias Toward Drug Approvals," *Washington Post*, August 9, 2006, available online at <http://www.washingtonpost.com/wp-dyn/content/article/2006/08/28/AR2006082800984.html>.

⁷ "Stagnation or Innovation," FDA (March 2004), at <http://www.fda.gov/oc/initiatives/criticalpath/whitepaper.html>.

Food Safety

Since 1906, FDA has had responsibility for regulating the safety of most food products. Its authority has evolved over time to reflect advances in food science and to address problems that have arisen with either certain categories of food (i.e., infant formula) or specific food components (i.e., food additives).⁸ Several recent widely-reported outbreaks of food borne illness have affected hundreds of individuals,⁹ and focused congressional attention on food safety. Many members have expressed concern with both domestic and imported food products. Food safety provisions in S. 1082 begin to address some of the larger issues in food safety reform that Congress may consider.

S. 1082 and H.R. 2900

The two comprehensive FDA reauthorization and reform bills address many, but not all of the same topics, though not always in the same way. (See **Table 1**). The remaining sections of this report contain descriptions of the key FDA programs addressed in the bills, certain programs considered but not included in the bills, and links to relevant CRS reports. Topics include prescription drug user fees, medical device user fees, pediatric drugs and devices, drug safety, clinical trials databases, conflicts of interest, importation of prescription drugs, Reagan-Udall Foundation, office of the chief scientist, food safety, and miscellaneous provisions in one bill or the other.

Table 1. Location of Various Subjects in S. 1082 and H.R. 2900

| SUBJECT | S. 1082 | H.R. 2900 |
|---|-------------------------|----------------------|
| Prescription Drug User Fees | Title I | Title I |
| Medical Device User Fees | Title III, Subtitle A | Title II, Subtitle A |
| Medical Device Regulation | Title III, Subtitle B | Title II, Subtitle B |
| Pediatric Exclusivity Incentives (BPCA) | Title IV, Subtitle A | Title V |
| Mandatory Pediatric Assessmts. (PREA) | Title IV, Subtitle B | Title IV |
| Pediatric Medical Devices | Title IV, Subtitle C | Title III |
| Drug Safety | Title II, Subtitle A, E | Title IX |
| Antibiotic Drugs | Title II, Subtitle F | Title IX |
| Clinical Trials Databases | Title II, Subtitle C | Title VIII |
| Conflicts of Interest | Title II, Subtitle D | Title VII |
| Reagan-Udall Foundation | Title II, Subtitle B | Title VI |
| Importation of Prescription Drugs | Title VIII and Title V | *** |
| Food Safety | Title VI and Title V | *** |
| Domestic Pet Turtle Market Access | Title VII | *** |

⁸ Infant Formula Act of 1980 ([http://www.congress.gov/cgi-lis/bdquery/R?d096:FLD002:@1\(96+359\)](http://www.congress.gov/cgi-lis/bdquery/R?d096:FLD002:@1(96+359))) and Food Additives Amendment of 1958 (P.L. 85-929).

⁹ CRS Report RL33722, *Food Safety: Federal and State Response to the Spinach E. coli Outbreak*, by (name redacted).

| SUBJECT | S. 1082 | H.R. 2900 |
|------------------|---------|-----------|
| Other Provisions | Title V | *** |

Prescription Drug User Fees

FDA's authority to collect user fees pursuant to the Prescription Drug User Fee Act (PDUFA; Section 735 of the Federal Food, Drug, and Cosmetic Act [FFDCA], 21 U.S.C. 379g) will expire on October 1, 2007, unless

Congress reauthorizes the program. First enacted in 1992, PDUFA gives FDA a revenue source—fees paid by pharmaceutical manufacturers—to supplement direct appropriations. At the time, FDA, consumers, and manufacturers all sought to shorten the time between a manufacturer's submission of an application and the agency's decision on whether to approve the product. Therefore, PDUFA restricted the use of collected funds to new product review, and established a mechanism for agency-industry collaboration to create performance goals that set targets primarily for review times.

For further information, see

CRS Report RL33914, *The Prescription Drug User Fee Act (PDUFA): History, Reauthorization in 2007, and Effect on FDA*, by (name redacted).

As a result of PDUFA, application review times decreased, and the addition of fee revenue raised the level of the premarket review activities relative to that for postmarket activities. Congress, therefore, in reauthorizing PDUFA in 1997 (PDUFA II) and 2002 (PDUFA III), gave FDA limited authority to use some of the fees for postmarket drug safety activities. Due, in part, to recent widely publicized safety problems with aggressively marketed drugs,¹⁰ discussions surrounding a 2007 PDUFA IV reauthorization have included an increased focus on postmarket drug safety.

Both S. 1082 and H.R. 2900 include, as Title I, the *Prescription Drug User Fee Amendments of 2007*. Both bills would reauthorize the assessment, collection, and use of three types of fees: application, establishment, and product fees. They would cover applications for both prescription and nonprescription drugs, eliminating the distinction in current law that covers only some nonprescription drugs.

Authorized Uses of Fees

The bills would add to the list of postmarket safety activities for which the fees could be used. Both would include adverse event data collection systems and improved analytical tools; the House bill list extends beyond the Senate's. Both the Senate and House bills would increase requirements for adverse event reporting, both to the HHS Secretary (Secretary) and to the public.

Authorized Fee Revenue

The Senate and House bills would both establish fee revenues, for each fiscal year, of \$393 million with various adjustments. They would amend the adjustment methods for inflation (to include cost of compensation and benefits) and workload (regarding active investigational new

¹⁰ For example, see Anna Wilde Mathews and Barbara Martinez, "Warning Signs: E-Mails Suggest Merck Knew Vioxx's Dangers at Early Stage," *Wall Street Journal*, November 1, 2004.

drug applications), and add an adjustment for rent and rent-related costs. The House, alone, would exempt from product and facility fees applications for orphan drugs marketed by companies with less than \$100 million in gross worldwide revenue in the preceding year.

New Fees for Advisory Review of Advertisements

Both bills would add a new §736A to the FFDCA to authorize the assessment and collection of fees to fund the advisory review of certain drug advertisements. Manufacturer requests for pre-release review of advertisements would be *voluntary* and FDA responses would be *advisory*. Only manufacturers that requested such reviews would be assessed the new fees, which would include an advisory review fee and an operating reserve fee.

Reauthorization and Report Requirements

The Senate bill would codify, within FFDCA §735, which it would rename as *Drug Fees*, certain core elements of the prescription drug user fee program that, although included in PDUFA I, II, and III, were never placed into the FFDCA. First, it would require the Secretary to submit annual performance and fiscal reports to Congress. Second, it would require the Secretary, in preparation for the next PDUFA reauthorization, to consult with congressional committees, scientific and academic experts, health care professionals, representatives of patient and consumer advocacy groups, and the regulated industry to develop recommendations for what would be PDUFA V, including goals and plans for meeting the goals. Expanding on PDUFA III, S. 1082 would require a public hearing and review of the Secretary's recommendations following its negotiations with the industry to set performance goals; and would require the Secretary to include with the submission to Congress a summary of the public comments and changes made to the recommendations in response to them.

The House bill would include the same reauthorization and report requirements but would not amend the FFDCA to include them. The House bill, alone, also would require that, before presenting recommendations to Congress, the Secretary make publicly available on the FDA website the minutes of all agency negotiations with the regulated industry and representatives of patient and consumer advocacy groups.

Medical Device User Fees

User fees were introduced into the medical device review process for the first time by the Medical Device User Fee and Modernization Act of 2002 (P.L. 107-250; MDUFMA). MDUFMA amended the FFDCA to enact three significant provisions for medical devices: (1) it established user fees for premarket reviews of devices; (2) it allowed establishment inspections to be conducted by accredited third parties; and (3) it instituted new regulatory requirements for reprocessed single-use devices. FDA's authority for the first of these (the collection of user fees) will expire on October 1, 2007, unless Congress reauthorizes it, as is proposed in S. 1082 (Title III), and H.R. 2900 (Title II). Both bills also contain certain other provisions related to the regulation of medical devices.

User Fee

The Medical Device User Fee and Modernization Act of 2002 (MDUFMA; 21 U.S.C. 379i, j) gave FDA the authority to collect user fees from manufacturers seeking FDA approval or clearance for their medical

devices. As noted above, that authority, and by reference, FDA's obligation to meet related performance goals, is set to expire on October 1, 2007, unless Congress reauthorizes it. Both S. 1082 and H.R. 2900 propose reauthorization through FY2012.

For further information, see

CRS Report RL33981, *Medical Device User Fee and Modernization Act (MDUFMA) Reauthorization*, by (name redacted).

S. 1082 and H.R. 2900 contain parallel provisions that would lower fee amounts for FY2008, include a subsequent 8.5% rise per year through FY2012, and add three new types of fees (annual establishment fees, registration fees, and 30-day fees). Both bills would except government entities from establishment fees (H.R. 2900 would extend this waiver to Indian tribes). For the newly created establishment fee, the Secretary could increase the fee amount in FY2010 up to an additional 8.5% over the annual 8.5% increase if fewer than 12,250 establishments paid the fee in FY2009.

Both bills would extend from FY2007 to FY2012 the requirement that there be a certain amount of medical device-related direct appropriations (at least \$205,720,000 multiplied by an annual adjustment factor) in order for the Secretary to assess fees, and be expected to meet performance goals. Both bills would amend a provision requiring that fees collected for a fiscal year that exceed the authorized appropriation be subtracted from fees authorized to be collected for the subsequent year. Instead, fees collected between FY2008 and FY2011 would be considered in aggregate. A reduction would be made in fees in the final year only if the amount collected in the four-year period exceeded the amount authorized for the same period. H.R. 2900 would also authorize the appropriation of specific sums from FY2009 FY2012 for the review of postmarket safety information on medical devices.

The bills would strike a provision that enables the Secretary to adjust the premarket notification fee amount annually so that, in aggregate, these fees comprise a target amount. However, H.R. 2900 would maintain a reference to this deleted provision in the *Fee Amounts* section (21 U.S.C. 379j(a)(2)(A)).

Regarding reduced or refunded fees, both bills would further reduce the fees paid by small businesses, remove a provision that the assets of partners and parent firms be considered in small business qualification, and enable foreign firms to qualify as small businesses. Both bills would also articulate a new refund policy specified for *modular applications*¹¹ withdrawn at different points before final FDA action is taken. S. 1082 specifies that the Secretary would have the sole authority to make refund decisions and that they are nonreviewable.

Both bills would require the Secretary to continue to file annual reports through FY2012. H.R. 2900 would require the reports to include information on postmarket safety activities. S. 1082 would require information on previous cohorts of medical device applications, would require that the reports be made public, and would write the report requirements into the FFDCA.

¹¹ A *modular application* is a medical device premarket application submitted to FDA over time, in parts.

In FDA's development of its performance goal recommendations to the Congress, both bills would require the agency (as did MDUFMA) to consult with an array of governmental, professional and consumer groups, publish its recommendations in the Federal Register, provide a public comment period, and hold a public meeting. S. 1082 would also specify that the recommendations be revised upon consideration of public comments, would require the recommendations' transmittal to Congress, and would write the relevant consultation requirements into the FFDCFA.

H.R. 2900's user fee provisions would take effect on the bill's date of enactment. S. 1082's provisions would become effective on October 1, 2007, and the bill also contains a related savings clause to help ensure continuity of fee collection.

Device Regulation

S. 1082 and H.R. 2900 would make other amendments related to medical device regulation. The bills generally contain parallel provisions (discussed below), except that H.R. 2900 would require the Comptroller General to conduct a study on nosocomial infections¹² relating to medical devices.

S. 1082 and H.R. 2900 would extend from FY2007 to FY2012 the authority to have third parties review premarket notifications. The bills also contain provisions that would revise the requirements for inspections by accredited third parties in three ways. First, by reducing administrative requirements associated with qualifying for the program. Second, by expanding participation in the program. Third, by permitting device companies to voluntarily submit to FDA reports by third parties assessing conformance with an appropriate international quality systems standard, such as those set by the International Standards Organization. FDA would consider the information in these reports in setting its inspection priorities.

Regarding required registration, both bills would restrict the period within which device producers must register with the Secretary from any time prior to December 31 of each year to between October 1 and December 31 of each year. The bills would also reduce from twice to once per year (between October 1 and December 31) the requirement that those who register with the Secretary provide a list of devices on which they perform specific functions.

Both bills would amend electronic registration regulations to require electronic filing as a default. However, S. 1082 contains a requirement that the Secretary find that the receipt of electronic information is feasible, which could require additional rulemaking.

Pediatric Drugs and Devices

FDA has approved for adult use many products never tested in children. Yet clinicians often prescribe them for children believing that the safety and effectiveness demonstrated with adults would hold for younger patients. However, this off-label prescribing can result in children receiving ineffective products, or too much or too little of a potentially useful drug. Some side

¹² A nosocomial infection is one a patient acquires in the hospital, and that was neither present nor incubating prior to the patient receiving services.

effects are unique to children or children of specific ages, including effects on growth and development. Studies show that, depending on the maturation and development of a child's organs and other factors, some drugs vary in how long they stay in the body, affecting their usefulness.¹³

With the Better Pharmaceuticals for Children Act (BPCA; included in FDAMA of 1997), Congress provided drug manufacturers with the following incentive to conduct pediatric use studies on their patented products: if a manufacturer complied with a written FDA request for a specific pediatric study, FDA would add six months to its market exclusivity for that product.¹⁴ For drugs no longer covered by patent or other marketing exclusivity agreements, BPCA required the Secretary to list those off-patent products for which pediatric studies are needed to assess safety and effectiveness. It also authorized the appropriation of National Institutes of Health (NIH) funding for these studies. For on-patent drugs whose manufacturers declined FDA's written requests for pediatric use studies, BPCA provided for their referral by FDA to the Foundation for the NIH.¹⁵ The Best Pharmaceuticals for Children Act (also BPCA) reauthorized the exclusivity provisions for another five years. They are set to expire on October 1, 2007.

For further information, see

CRS Report RL33986, *FDA's Authority to Ensure That Drugs Prescribed to Children Are Safe and Effective*, by (name redacted).

CRS Report RL33288, *Proprietary Rights in Pharmaceutical Innovation: Issues at the Intersection of Patents and Marketing Exclusivities*, by (name redacted).

In 1998, FDA published the Pediatric Rule, which mandated that manufacturers submit pediatric testing data, referred to as a pediatric assessment, at the time of all new drug applications. In 2002, a federal court declared the rule invalid, holding that FDA lacked the statutory authority to promulgate it. Congress gave FDA that authority with the enactment of the Pediatric Research Equity Act of 2003 (PREA; P.L. 108-155). PREA covers drugs and biological products and includes provisions for deferrals, waivers, and the required pediatric assessment of an approved marketed product. PREA did not include a specific sunset date; its provisions remain in effect as long as BPCA is authorized.

Pediatric Exclusivity Incentives (BPCA Reauthorization)

Both S. 1082 (Title IV, Subtitle A) and H.R. 2900 (Title V) would reauthorize BPCA (FFDCA §505A) for another five years, through FY2012. The bills also would encourage research on off-patent products, strengthen the requirements for labeling changes based on the results of pediatric use studies, and provide for the reporting of adverse events. A key difference between the Senate and the House bills concerns the period of exclusivity, which is six months in current law. While H.R. 2900 would leave that provision unchanged, S. 1082 would reduce it to three months for drugs with over \$1 billion in annual gross U.S. sales.

¹³ William Rodriguez, Office of New Drugs, FDA, "What We Learned from the Study of Drugs Under the Pediatric Initiatives," June 2006 presentation to the Institute of Medicine, at <http://www.fda.gov/oc/opt/presentations/whatwelearned.ppt>.

¹⁴ During that six-month period, FDA would not grant marketing approval to another identical product (usually a generic).

¹⁵ The Foundation supports the research mission of NIH using public-private partnerships ("The Foundation for the NIH," at <http://www.fnih.org/aboutus/aboutus.shtml>).

Mandatory Pediatric Assessments (PREA Reauthorization)

S. 1082 (Title IV, Subtitle B) and H.R. 2900 (Title IV) would expand FDA's authority under PREA (FFDCA §505B), which requires pediatric assessments of new drugs and biologics or, for example, new indications of marketed products, by strengthening standards for requiring tests, explanation of deferrals, labeling, and publicly accessible information. In one key difference between the two bills, H.R. 2900 would eliminate the provision that ties PREA's authorities to BPCA authorization; S. 1082 would maintain that connection.

Pediatric Medical Devices

In addition to reauthorizing BPCA and PREA, both S. 1082 (Title IV, Subtitle C) and H.R. 2900 (Title III) incorporate legislation that is intended to encourage medical device manufacturers to develop pediatric products. The *Pediatric Medical Device Safety and Improvement Act of 2007* would amend FFDCA by modifying the *humanitarian device exemption* (HDE), which allows a manufacturer with a device aimed at a U.S. patient population of less than 4,000 to market the product without having to demonstrate its effectiveness (only its safety), and to have certain application fees waived. The exemption from proving effectiveness is designed to encourage manufacturers to develop medical devices for these small markets, assisting patients with rare diseases and conditions who might otherwise not be served. Specifically, the legislation would exempt some manufacturers of pediatric devices for small populations from the general HDE prohibition on selling a device for an amount that exceeds its costs of research and development, fabrication, and distribution. The bills contains similar, though not identical, inspection authorities, and guidance and reporting requirements related to the new exemption. S. 1082 would extend the new exemption through 2012. H.R. 2900 would extend it through 2013.

Regarding funding for research on pediatric medical devices, both bills would require the NIH Director to designate a contact point or office to help pediatric medical device developers locate funding. H.R. 2900 would also require the FDA Commissioner, in collaboration with other agency heads, to submit a plan for expanding pediatric medical device research and development to relevant congressional committees.

Both bills would require the Secretary to establish a demonstration project to promote pediatric device development. The bills' descriptions of use of grant funds are not identical, but both focus on possibilities such as connecting innovators with manufacturers, managing the device development process, connecting innovators to federal resources, and providing business assistance. Both bills would require coordination with appropriate points of contact at NIH and FDA. S. 1082 would also require grantees to report their effectiveness, impact, and device development status to the Secretary annually. For the demonstration grants, both bills would authorize \$6 million for each of FY2008 through FY2012.

Both bills would amend BPCA to expand the focus of the Office of Pediatric Therapeutics (OPT) and the Pediatric Advisory Committee to include pediatric medical devices. S. 1082 would also require the OPT, in collaboration with the heads of relevant agencies, to deliver a plan for expanding pediatric medical device research and development to relevant congressional committees.

Finally, both bills would amend the FFDCA to incorporate certain postmarket surveillance measures. They would expand the Secretary's authority, enabling postmarket studies to be

required as a condition of approval for pediatric medical devices that require safety controls (class II or III devices). H.R. 2900 specifies that such studies may be required for devices indicated for pediatric populations; both bills indicate they may be required for devices expected to have significant use in pediatric populations, and that studies may exceed the general 36-month limitation if necessary to assess the impact of the device on pediatric populations' growth and development. H.R. 2900 also includes a dispute resolution provision, entitling a manufacturer to request a review, during which the device may not be deemed misbranded except as necessary to protect public health.

Drug Safety

Since the 1938 passage of the *Federal Food, Drug, and Cosmetic Act*, the manufacturer of a new drug has had to demonstrate to FDA the product's safety before FDA would approve it for marketing in the United States. In 1962, the *Harris-Kefauver Amendments* to the FFDCA added product effectiveness to the premarket requirements. The *Prescription Drug User Fee Act* of 1992 maintained the focus on premarket review. However, as previously noted, until a very large number of individuals have taken a drug, a rare adverse effect may not occur or a very common condition may not be recognized as drug-associated. FDA, therefore, cannot assert that any drug is completely safe. Instead, it considers whether, given the available information, the drug is safe enough when used correctly by the types of individuals and for the diseases or conditions for which it was tested. FDA and others must remain alert to new information as those drugs are used more widely. In recent years, researchers revealed that a few widely used (and advertised) drugs were more dangerous than known or expected. Some felt that the public health and regulatory problems were compounded by questions about: (1) industry's reticence in sharing its knowledge of possible risks; and (2) FDA's authority, ability (resources), and willingness to identify and correct postmarket safety concerns. As a result, FDA asked the Institute of Medicine (IOM) to examine its handling of drug safety. IOM responded with a 2006 report that addressed the agency's organizational culture, science and expertise, regulation, communication, and resources.¹⁶ At the same time, many consumers, health experts, and Members of Congress looked for ways to enhance FDA's actions to protect the public.

For further information, see

CRS Report RL32797, *Drug Safety and Effectiveness: Issues and Action Options After FDA Approval*, by (name redacted).

S. 1082 (Title II, Drug Safety) and H.R. 2900 (Title IX, Enhanced Authorities Regarding Postmarket Safety of Drugs) reflect those concerns. They would establish some new authorities and expand others to allow FDA to identify postmarket drug safety problems and to correct or minimize them.

Active Surveillance and Assessment

Although the Senate and House bills differ on timetables and organization, both would require that the Secretary establish public-private partnerships to develop a postmarket risk identification and analysis system using electronic databases.

¹⁶ Institute of Medicine, Committee on the Assessment of the U.S. Drug Safety System, *The Future of Drug Safety: Promoting and Protecting the Health of the Public*, Alina Baciou, Kathleen Stratton, Sheila P. Burke, Editors, (Washington, DC: National Academies Press, 2006) at <http://www.nap.edu/catalog/11750.html>. (Hereinafter, "IOM, 2006.")

Risk Evaluation and Mitigation Strategies

Current law allows FDA to require a postmarket study as a condition of its initial approval of a marketing application. The law does not authorize FDA to add such requirements after approval, though FDA does recommend that postmarket studies be conducted for products on the market. Many observers believe that such recommendations and requests do not create enough needed postmarket studies.¹⁷ Thus, the Senate and House bills propose a strengthened authority and set of procedures to support FDA's postmarket safety activities.

At the core would be a Risk Evaluation and Mitigation Strategy (REMS). Both bills would authorize the Secretary to require that the sponsor of a drug or biologic application or supplement to an application submit a proposed REMS. The bills differ on the criteria they would require that the Secretary use. The House bill language calls for pre-approval "to ensure that the benefits of the drug involved outweigh the risks of the drug." The Secretary could require a REMS after a product has been approved if the Secretary "becomes aware of new safety information," based, in part, on the sponsor's required statement as part of the application of whether it believes a REMS or a postmarket study or clinical trial should be required. The Senate bill requires that the Secretary's determination be "based on a signal of a serious risk with the drug" and that a REMS is necessary "to assess such signal or mitigate such serious risk."

This authority also would cover supplemental applications concerning a new indication for use of an approved product and applications for the marketing of a generic product.

Both bills call for all REMS to include certain core elements, including timeframes, and other elements that the Secretary could require. Elements might include instructions to patients and clinicians, and restrictions on distribution or use (and a system to monitor their implementation). Both bills would allow a waiver from REMS restrictions on distribution or use for certain medical countermeasures in the time of a declared public health emergency. The Senate bill would create a mechanism to assure access to a drug with a REMS for off-label use for a serious or life-threatening disease or condition.

Most elements considered in a REMS are part of current FDA practice. The REMS process proposed by S. 1082 and H.R. 2900 would add authority for structured follow-through, dispute resolution, and enforcement. Both bills would require reviews of approved REMS at specified times initially and then as the Secretary would determine. They lay out detailed procedures for the review of both proposed REMS and required or voluntary assessments or modifications. Both the Senate and the House bills would establish a Drug Safety Oversight Board, made up of federal government scientists and health care practitioners, which would participate in resolving disputes between the Secretary (through FDA scientists) and a product's sponsor.

The bills would require the Secretary, through the Drug Safety and Risk Management Advisory Committee, to evaluate whether the various REMS elements assure safe use of a drug; and whether they limit patient access or place an undue burden on the health care system.

¹⁷ IOM, 2006.

Postmarket Studies

Both bills would authorize the Secretary to require postapproval studies or clinical trials, but they differ on the criteria for determining whether they are necessary. According to the Senate bill, the Secretary, in addition to routine active surveillance and other requirements, would have “to assess a signal of a serious risk with use of a drug; or to identify, based on a review of a demonstrated pattern of use of the drug, unexpected serious risks in a domestic population....” The House bill, unlike S. 1082, addressing this outside of the REMS process, would authorize the Secretary to require, based on scientific information, a postapproval study to assess a known risk, assess signals of serious risk, or to identify a serious risk.

Labeling

The Senate bill would require the sponsor and the Secretary to notify each other upon acquiring new safety information that they think should be included in a drug’s labeling. For times when a sponsor disagrees with the Secretary’s request to prepare a supplemental application to change the labeling, the bill would set up a multi-level process, with defined time limits, involving meetings, dispute review and recommendations by the Drug Safety Oversight Board, and, if the Secretary determines necessary, an order to make the safety labeling change. If the sponsor continues to disagree, the Secretary may deem the drug to be misbranded.

The House bill would authorize the Secretary, based on new safety information, to order a labeling change. Both bills include time limits for sponsor and Secretary; the labeling provisions also include a dispute resolution procedure.

Advertising

Both bills would authorize the Secretary to require submission of certain advertisements to the Secretary for review before dissemination, although they set different criteria for the Secretary’s decision. The House bill refers to television ads and specifies that the Secretary could recommend but not require changes. The Senate bill refers to advertisements, not distinguishing among the media. Both bills would require a “clear and conspicuous presentation of side effects and contraindications.”

Enforcement

By allowing the Secretary to impose civil monetary penalties for violations of certain requirements, both bills would give FDA a new enforcement tool. For violating a REMS, both bills would authorize fines of up to \$250,000 (the Senate also would set a \$15,000 minimum) per violation, and up to \$1 million for violations adjudicated in a single proceeding. The House bill would include additional civil penalties if a violation were to continue after the Secretary had provided notice: \$10 million per violation, not to exceed \$50 million for all violations adjudicated in single proceeding. For a violation that is continuing in nature and poses a substantial threat to public health, the Secretary could fine the sponsor up to \$1 million per day.

Both bills would allow the Secretary to consider a drug not in compliance with certain elements of its REMS to be misbranded. The House bill explicitly states that a sponsor could not market a product with a REMS if it is not in compliance with REMS.

The Senate and House bills would establish separate civil penalty authority for the dissemination of a false or misleading direct-to-consumer (DTC) ad for a prescription drug. The House bill fine for a first violation would be up to \$250,000, with fines for subsequent violations not to exceed \$500,000 each. The Senate bill would authorize lower fines: up to \$150,000 for a first violation and up to \$300,000 for subsequent violations.

Funding

Both bills would authorize increased appropriations to support components of the proposed drug safety provisions. For the *surveillance and assessment activities*, both would authorize the Secretary to use \$25 million of PDUFA fees each year to carry out those activities. For *REMS and other drug safety activities* in this title, the Senate bill would increase the revenue allowed under PDUFA by \$225 million over FYs 2008 through 2012, and designate its use for drug safety activities. The House bill would authorize appropriations of \$125 million for that five-year period (i.e., \$25 million annually).

Antibiotic Drugs

The House bill would require the Secretary to issue guidance for the conduct of clinical trials of antibiotic drugs, and require the Secretary to convene a public meeting regarding orphan antibiotic products. It would also authorize appropriations of \$30 million for each of the next five FYs for grants and contracts to develop orphan drugs. The Senate bill would consider antibiotics as orphan products and authorize \$35 million for each of those fiscal years. The Senate bill includes other provisions regarding antibiotic access and innovation; one would provide incentives (extended marketing exclusivity) for the development of certain antibiotics.

Anti-Counterfeiting Technologies

The Senate bill would require, within a specified timeframe, that the packaging of any prescription drug incorporate a standardized numerical identifier and overt optically variable counterfeit-resistant technologies. The House bill would require the Secretary to develop standards and evaluate technologies to secure the distribution system against prescription drugs that are counterfeit, diverted, or substandard or damaged.

Drug Safety Provisions In Only One Bill

Some drug safety provisions appear in only one or the other bill. Many are reports to Congress on the implementation of a provision, or studies of options or effectiveness regarding drug safety.

In H.R. 2900 Alone

The House bill would require that any DTC ad include the following statement: “You are encouraged to report adverse effects of prescription drug medication to the FDA. Log onto <http://www.fda.gov/medwatch> or call 1-800-FDA-1088.”

In S. 1082 Alone

Within the “drug safety” title of the Senate bill, provisions would require that the Secretary establish an *Advisory Committee on Risk Communication*; and develop and maintain *website content* to include an extensive range of drug safety information, including summaries of surveillance data, and documents from drug approval and biologics licensing applications such as a summary of conclusions from all reviewing disciplines and staff disagreements and recommendations.

The Senate bill would also require that state-legalized *medical marijuana* be subject to FDA’s full regulatory requirements. In addition, upon the approval of a neglected or tropical disease product, it would require the Secretary to award to its sponsor a *priority review voucher*, which that sponsor may transfer (including by sale) to a sponsor of a new drug application; the recipient of the voucher would then be eligible for priority review of a new drug application. It would require the FDA Commissioner to create and publish on the FDA website a *list of all authorized generic drugs*, and set up a procedure to prevent certain *citizen petitions* from delaying agency decisions without review by the Secretary.

Clinical Trials Databases

Federal registration requirements for clinical trials were created by §113 of the Food and Drug Administration Modernization Act of 1997 (FDAMA), which amended §402 of the Public Health Service Act (42 U.S.C. 282; PHSA). Registration is currently required for clinical trials of drugs (but not biologics or medical devices) intended to treat serious or life-threatening diseases and conditions. The current registry is available online at *clinicaltrials.gov*. S. 1082 (Title II, Subtitle C) and H.R. 2900 (Title VIII) contain proposals to expand both the types of trials and types of information about the trials in the registry (either expanding or supplanting *clinicaltrials.gov*). They also contain provisions requiring the publication of the results of many clinical trials.

For further information, see
 CRS Report RL32832, *Clinical Trials Reporting and Publication*, by (name redacted).

Registry

S. 1082 and H.R. 2900 would require the registration of most clinical trials involving drugs, devices and biologics—not just those involving treatments for life-threatening conditions—and would include international trials on products with or seeking FDA approval. However, H.R. 2900 would forestall the public release of registry-submitted medical device information until after FDA had cleared or approved the device. S. 1082 would exempt newly created pediatric postmarket surveillance clinical trials from registry requirements, and would allow the voluntary registration of clinical trials that are not required to be submitted. Both bills would link the timing of certain requirements to the trial’s completion date. H.R. 2900 would link the definition of *completion date* to the collection of data relevant to primary and secondary outcomes.

Both bills would require the *responsible party* (RP) for a trial—the trial sponsor or possibly principal investigator—to comply with the bills’ provisions. Both bills articulate certain requirements for when a principal investigator might serve as RP; however, only H.R. 2900

would require that a principal investigator have control over the data and a right to publish trial results in order to serve as RP.

Both bills would expand the type of information that must be included in the registry and made public via the Internet, would dictate that it be searchable in specific ways, and would require that no item or fact submitted be false or misleading. Both bills would require submitted information to include the elements of the World Health Organization's International Clinical Trials Registry Platform registration data set and other elements.¹⁸ H.R. 2900 would require a few elements not required by S. 1082, including the disclosure of agreements that restrict non-employees from discussing or publishing trial results.

H.R. 2900 would require that updates, reflecting the dates of any changes, be submitted to the registry once every six months until the results of the trial were submitted to the results database. S. 1082 specifies a few more criteria than does H.R. 2900 by which the registry must be searchable, including, for example, the age group studied in the trial. S. 1082 also specifies a timeline by which the NIH Director must make registry information public, and would require the registry to link to certain public clinical trial results information, for example from FDA and NIH.

Results Database

Both H.R. 2900 and S. 1082 have provisions related to the establishment of a public database containing the *results* of clinical trials. However, only H.R. 2900 provides specific instructions on the creation of the results database. S. 1082, in contrast, would require the Secretary to create a database through rulemaking, based on the recommendations of the NIH Director. H.R. 2900 specifies for the results database certain searchable categories, the timing of required submissions and their public posting, and that the information submitted be truthful and regularly updated. A requirement that results summaries be non-promotional was removed from an earlier draft of the bill, and replaced by a requirement that the Comptroller General conduct a study and report to Congress on whether information in the results database is promotional.

Regarding the timing of posting into the results database, H.R. 2900 would require that the results of pre-approval studies be made public within 30 days of a number of possible events, including the Secretary issuing a *not substantially equivalent* (NSE) letter regarding a medical device.¹⁹ The issuance of an NSE letter does not necessarily mark the conclusion of an FDA application for a device manufacturer; a manufacturer may opt to apply to FDA for *premarket approval*.²⁰ Thus, the timing provision could result in clinical trial information being made public regarding a device for which FDA action was still pending. A parallel provision regarding studies pertinent to a new use of a drug or device already on the market does raise the same issue. It would allow for a posting delay of up to two years if the manufacturer certified to the Secretary that a filing with FDA for a new use would soon be made.

¹⁸ "The World Health Organization announces new standards for registration of all human medical research," World Health Organization website, May 19, 2006, at <http://www.who.int/mediacentre/news/releases/2006/pr25/en/index.html>, visited July 18, 2007.

¹⁹ The least rigorous pathway that a manufacturer may use to gain FDA permission to market a medical device is to demonstrate that it is very similar to—or *substantially equivalent* (SE) to—a product already on the market. FDA will issue an NSE letter if it finds that a product is different from, not substantially equivalent to, one on the market.

²⁰ An application for *premarket approval* is more rigorous than an application to demonstrate SE, and is required for devices that are novel and/or require certain safety controls.

Coordination, Compliance, and Enforcement

Both bills include coordination, compliance, and enforcement provisions. H.R. 2900's compliance provisions would apply to registry and results database requirements, whereas parallel provisions in S. 1082 would only apply to registry provisions. H.R. 2900 contains provisions regarding enforcement of results database requirements and coordination between registry and results database, and would prohibit the Secretary from filing, approving, or clearing FDA applications with noncompliant trials. S. 1082 would require FDA applications to include certification of registry requirement compliance. One controversial provision that was dropped from H.R. 2900 (and was never present in S. 1082) specified that the act would not have had any legal effect on—and thus would have allowed—causes of action for damages under state law.

Current law does not specify penalties or enforcement mechanisms related to registry requirements. General mechanisms for enforcing compliance with FDA requirements may be applicable, but have not been applied by the FDA. Both H.R. 2900 and S. 1082 contain specific penalties for noncompliance. In its enforcement provisions, H.R. 2900 refers to but would not amend relevant FFDCAs, allowing penalties of \$10,000 per day, and capping penalties at \$15,000 for individuals and nonprofits. S. 1082 would amend relevant FFDCAs and would allow penalties of \$10,000 for a first violation, and up to \$20,000 for subsequent violations.

Conflicts of Interest

Both S. 1082 (Title II, Subtitle D) and H.R. 2900 (Title VII) contain provisions that would affect FDA's treatment of conflicts of interest in its advisory committees. Current law

generally requires that committee members be free from conflicts of interest, but allows for exceptions to that rule under specific circumstances. Under FDA's current approach, a conflict of interest may require a potential committee member to disclose the conflict, refrain from voting, and/or not participate in a committee, depending on the nature of the conflict. The law is articulated primarily in three sources: (1) the Federal Advisory Committee Act (5 U.S.C. Appendix; FACA); (2) the FDA advisory committee policy (21 U.S.C. 355(n)); and (3) a law governing *special government employees*—which advisory committee members are—*Acts Affecting Personal Financial Interest* (18 U.S.C. chapter 11, §208).²¹ S. 1082 and H.R. 2900 would both insert a new provision into Chapter VII Subchapter A of the FFDCAs, effective October 1, 2007, that would change both the process of recruiting advisory committee members, as well as some circumstances under which and processes by which conflict-of-interest waivers may be granted. The new provisions would also cause some requirements currently only applicable to drug and biologic advisory committees to apply to committees providing advice on all topics.

Both bills define *advisory committee* as a FACA-covered entity that provides the Secretary with advice and recommendations regarding activities of the FDA, and define *financial interest* as defined under 18 U.S.C. 208(a). This definition covers activities such as a person's or their family

For further information, see

CRS Report RS22691, *FDA Advisory Committee Conflict of Interest*, by (name redacted).

²¹ For more information, see CRS Report R40520, *Federal Advisory Committees: An Overview*, by Wendy R. Ginsberg.

members' current or future employment, trusteeship, or directorship. On its face, it does not apply to activities such as stock ownership, former employment, or receipt of a grant or contract, although FDA's regulations do require disclosure of these types of activities. An alternative definition, offered in 21 U.S.C. 355(n), has been interpreted to require disclosure relating to a broad range of activities, including those listed above. However, as encoded in statute, this definition applies only to drug and biologics committees, not to medical device committees.

S. 1082 and H.R. 2900 would require advisory committee member recruitment mechanisms, generally focused on reaching experts from areas such as academia, medical research institutions, public interest and consumer groups. Both contain provisions to discourage financial conflict waivers. H.R. 2900 contains a section that would specifically permit the participation of a non-voting guest expert with financial interest if the Secretary determined that the guest had particular required expertise.

S. 1082 and H.R. 2900 would require advisory committee members' full financial disclosure prior to a meeting on a related matter. They would preclude voting by a member with a conflict of interest unless exempted by the Office of Government Ethics. The bills would allow a waiver of the voting restriction if necessary to provide the committee with essential expertise. H.R. 2900 would only allow one such waiver per meeting.

The bills would require public disclosures for conflict-of-interest determinations, certifications, and waivers, and would require the Secretary to submit annual reports regarding advisory committee membership, and conflict-of-interest waivers. Both bills would require the Secretary to review and update FDA conflict-of-interest guidance not less than once every five years.

Reagan-Udall Foundation for the Food and Drug Administration

S. 1082 (Title I, Subtitle B) and H.R. 2900 (Title VI) would establish a nonprofit corporation to advance FDA's mission regarding product development, innovation, and safety. The initial Board of Directors (the FDA Commissioner, and the directors of NIH, CDC, and AHRQ) would select the appointed members from a National Academy of Sciences-provided candidate list and then resign from the board. The ongoing board would include representatives from industry, academic research organizations, government agencies, patient or consumer advocacy organizations, and health care providers. The Foundation would establish goals and priorities relating to unmet needs and then coordinate with federal programs, and award grants, contracts, and other agreements with public and private individuals and entities to advance those goals. The House and Senate bills would direct the Commissioner to transfer between \$500,000 and \$1,250,000 to the Foundation.

Office of the Chief Scientist

The Senate and House bills would require the Secretary to establish an Office of the Chief Scientist within the FDA Office of the Commissioner. Among the duties of the Secretary-appointed Chief Scientist would be to oversee, coordinate, and ensure quality and regulatory focus of FDA's intramural research programs.

Miscellaneous Provisions in S. 1082

S. 1082 contains a number of provisions that are not present in H.R. 2900, as described below.

Importation of Prescription Drugs

Current law prohibits the importation of a prescription drug by anyone other than its manufacturer. S. 1082 (Title VIII, the *Pharmaceutical Market Access and Drug Safety Act of 2007*) would allow commercial and personal-use importation. The provision would create a detailed set of procedures to address concerns relating to the safety and effectiveness of imported drugs, cost savings to U.S. consumers, and

administration of the program. The Senate voted to add the provision to the bill during Senate consideration. However, the Senate also added a second-degree amendment, specifying that the title would become effective only if the HHS Secretary certified to Congress that its implementation would: (1) pose no additional risk to the public's health and safety; and (2) result in a significant

reduction in the cost of covered products to the American consumer. The addition of the second-degree amendment effectively nullified the language of the rest of the title, as both the current and former Administration have refused to make such a certification.

For further information, see

CRS Report RL32511, *Importing Prescription Drugs: Objectives, Options, and Outlook*, by (name redacted).

CRS Report RS22660, *Prescription Drug Importation: How S. 242 / H.R. 380 Would Change Current Law*, by (name redacted).

CRS Report RL32191, *Prescription Drug Importation: A Legal Overview*, by (name redacted).

Food Safety

The topic of food safety is addressed in S. 1082 in both Title VI—*Food Safety*, and in several sections of *Title V—Other Provisions*. H.R. 2900 contains no food provisions.

Title VI of S. 1082 would require that regulations be established on the processing and ingredient standards for pet food, animal waste and ingredient definitions, and on updated standards for nutrient and ingredient information on pet food labels. It would also

require that an early warning and surveillance system be established to identify adulteration of the pet food supply and outbreaks of disease associated with pet food. During a recall of either human or pet food, the Secretary would be required to collect and aggregate information on the recall, use existing communication networks to effectively alert the public, and post recall information on the FDA website. The Secretary also would be directed to coordinate activities, provide assistance and support staff training for states to improve food safety programs for fresh and processed produce, including attention to retail commercial food establishments, and establish procedures and requirements for processed produce.

For further information, see

CRS Report RS22600, *The Federal Food Safety System: A Primer*, by (name redacted).

CRS Report RL33559, *Food Safety: National Uniformity for Food Act*, by (name redacted).

Title VI of S. 1082 would also amend §417 of the FFDCA, by requiring the creation of a registry on adulterated food in which instances of reportable adulterated food may be listed. The Secretary would be required to review and determine the validity of the information received before

submitting them to the registry and exercising any other food authority action to protect the public. Alerts would be issued to the public for food that either had been associated with repeated, separate outbreaks of illness or adulteration, or that was a reportable adulterated food. The responsible party or importer of an adulterated food would be responsible for maintaining records on the problem and reporting to FDA once a determination of adulteration was reached. Any situation in which the Secretary determined that a deliberate adulteration had occurred would also have to be reported to the Department of Homeland Security.

The Secretary would be required to promulgate regulations and establish standards and thresholds for reporting instances of suspected reportable food adulteration and notification procedures. The bill would also require an annual report to Congress on the number and amount of food imports, food import inspectors and inspections, and the violations and enforcement actions taken. Nothing in the provisions would affect the regulation or the adverse event reporting system for dietary supplements under the Dietary Supplement Health and Education Act of 1994 (P.L. 103-417) or the Dietary Supplements and Nonprescription Drug Consumer Protection Act (P.L. 109-462), respectively.

Certain provisions in S. 1082 Title V would require the preparation of reports on the following food issues: pesticide residue monitoring program; whether substances used to preserve the appearance of fresh meat pose health hazards or mislead consumers; the color additive certification program's performance and financial status; any environmental risks associated with genetically engineered seafood products; the marketing of certain crustaceans; the detection and assessment of risks; and the authorization of appropriations as needed to implement an inspection regime for aquaculture and seafood. An additional food provision in this title includes the prohibition on importing from any foreign food facility that denies access to U.S. inspectors. Finally, authorization would be provided for enhancing the FDA inspection regime for aquaculture and seafood through partnerships.

Other Provisions

S. 1082 includes a number of additional provisions that are not present in H.R. 2900. For example, S. 1082 has a title (Title VII—*Domestic Pet Turtle Market Access*) that would enable the sale of pet turtles if specific requirements are met for sanitization and information disclosure to buyers. Other provisions would require an Institute of Medicine report on *genetic test safety and quality*, and an FDA report on *indoor tanning* device labeling, and the link between tanning device use and skin cancer.

S. 1082 includes two provisions expressing the sense of the Senate. One states that legislation should be passed that allows the FDA appropriate flexibility in the regulation of *follow-on biologics*. The second would express the Senate's sense that the Trade Representative should use all available tools to address violations and other concerns with *intellectual property*, and develop and submit to Congress a strategic plan to address the problem of countries that infringe upon American pharmaceutical intellectual property rights and/or engage in price manipulation.

Miscellaneous Provision in H.R. 2900

A provision considered only in the House bill addresses another public-private partnership. The House bill would require the Secretary, through the FDA Commissioner, to enter into

collaborative agreements (*Critical Path Public-Private Partnerships*) with educational or tax-exempt organizations to implement the FDA Critical Path Initiative “by developing innovative, collaborative projects in research, education, and outreach for the purpose of fostering medical product innovation, enabling the acceleration of medical product development, and enhancing medical product safety;” and authorizes to be appropriated \$5 million for FY2008 and such sums as may be necessary for each of FYs 2009 through 2012.

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