FDA Amendments Act of 2007 (P.L. 110-85)

Erin D. Williams
Specialist in Public Health and Bioethics

Susan Thaul
Specialist in Drug Safety and Effectiveness

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Summary

On September 27, 2007, the Food and Drug Administration Amendments Act of 2007 (FDAAA; H.R. 3580) was signed into law (P.L. 110-85). The comprehensive law reauthorizes four expiring Food and Drug Administration (FDA) programs and expands the agency's authority to regulate the safety of prescription drugs and biologics, medical devices, and foods. Understanding the way in which FDAAA changed the law governing the agency informs policy discussions aimed at additional FDA reform and reorganization, as well as those related more broadly to the quality, availability, and cost of medical products in the health care system.

At its core, FDAAA renews the authority for two key user fee programs that were 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). In FY2007, the year in which FDAAA was enacted, these programs accounted for 91% of FDA's user fee revenue and 18% of FDA's total budget. Without the reauthorizations, and absent a substantial increase in FDA's annual appropriations, the agency would have lost a significant amount of funding.

In addition to user fee programs, FDAAA reauthorizes two other FDA authorities related to prescription drugs for pediatric populations, which were 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 drugs. FDAAA also contains provisions related to drug safety, pediatric medical devices, clinical trial databases, the creation of a new nonprofit entity to assist FDA with its mission, and food safety.

This report presents a detailed summary of provisions in FDAAA. Each section of the report begins with background information about the FDA relevant to the passage of FDAAA and some references, if appropriate, to the two bills that formed its basis (S. 1082 and H.R. 2900), and a law that amended it (P.L. 110-316); describes FDAAA's contents; and analyzes how FDAAA changed the law. The report also contains links to pertinent CRS reports. This report, which is intended for reference use, will not be updated other than to reflect any technical changes that Congress might enact.

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Title IV. Pediatric Research Equity Act of 2007

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 products that do not work for them, or receiving too much or too little of a potentially useful drug. 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. Some side effects are unique to children or children of specific ages, including effects on growth and development.[16]

Recognizing the obstacles (which could be economic, ethical, legal, or mechanical) that make manufacturers reluctant to conduct research to address these questions, FDA and Congress developed two approaches to facilitate pediatric research. FDAAA continues both programs. The first, the Pediatric Research Equity Act (FDAAA Title IV, discussed in this section) is a mandatory program that requires pediatric assessments as part of every new application regarding a new ingredient, indication, dosage form, dosing regimen, or route of administration. The second, the Best Pharmaceuticals for Children Act (FDAAA Title V, discussed in the following section of this report) is voluntary, offering a six-month marketing exclusivity for a product in return for pediatric studies.

> For further information, see CRS Report RL33986, *FDA's Authority to Ensure That Drugs Prescribed to Children Are Safe and Effective*, by Susan Thaul.

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.[17] Congress gave FDA that authority with the enactment of the Pediatric Research Equity Act of 2003 (PREA; P.L. 108-155). PREA requirements cover all drug and biological product applications or supplements to applications concerning a new active ingredient, new indication, new dosage form, new dosing regiment, or new route of administration. The Act includes provisions for deferrals and waivers. PREA also authorizes the Secretary to require the sponsor of an already approved and marketed drug or biological product to submit a pediatric assessment based on criteria described in the law.

The Pediatric Research Equity Act of 2007, Title IV of FDAAA, reauthorizes PREA, amending it to strengthen standards for required tests, explanation of deferrals, labeling, and publicly accessible information. PREA now requires the Secretary to establish an internal committee, composed of FDA employees with specified expertise, to participate in the review of pediatric plans and assessments, deferrals, and waivers. The law requires the Secretary to track assessments and labeling changes and to make that information publicly accessible; establishes a dispute resolution procedure, which allows the Commissioner, after specified steps, to deem a drug to be

[16] 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.

[17] See Association of Am. Physicians and Surgeons, Inc. v. United States Food and Drug Admin., 2002 U.S. Dist. LEXIS 19689 (October 17, 2002).

misbranded if a manufacturer refuses to make a requested labeling change; and includes review and reporting reporting requirements for adverse events.

PREA requires reports from both the Institute of Medicine (IOM) and the Government Accountability Office (GAO). It also continues to link the program's authorization to the five-year authority FDAAA provides to the pediatric exclusivity program. (See discussion of FDAAA Title V in the next section of this report.)

Table 6. Comparison of *Pediatric Research Equity Act of 2007 (FDAAA Title IV)* with Previous Law

Topic	Previous Law	FDAAA Title IV
Authority Regarding New Drugs and Biological Products	A person submitting an application (or a supplement to an application) to market a drug or biologic with a new active ingredient, new indication, new dosage form, new dosing regimen, or new route of administration must submit with the application a pediatric assessment. [FDAAA 402(a); FFDCA 505B(a)(1); 21 USC 355c]	
		The reauthorizing law specifies that this Act applies to applications submitted on or after the date of FDAAA's enactment. [FDAAA 402(a); FFDCA 505B(a)(1); 21 USC 355c]
	The assessments must contain data, gathered using appropriate formulations *for each age group* for which the assessment is required, that are adequate to assess the safety and effectiveness of the drug or the biological product for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the drug or the biological product is safe and effective. [FDAAA 402(a); FFDCA 505B(a)(2); 21 USC 355c]	
	If the course of the disease and the effects of the drug are sufficiently similar in adults and pediatric patients, FDAAA authorizes the Secretary to judge pediatric effectiveness based on *extrapolation* from adequate and well-controlled studies in adults, usually supplemented with other information obtained in pediatric patients, such as pharmacokinetic studies. A study may not be needed in each pediatric age group if data from one age group can be extrapolated to another age group. [FDAAA 402(a); FFDCA 505B(a)(2)(B); 21 USC 355c]	
		A review for an application must include a brief *documentation* of data that support the extrapolation conclusions. [FDAAA 402(a); FFDCA 505B(a)(2); 21 USC 355c]

Topic	Previous Law	FDAAA Title IV
Authority Regarding Already Marketed Drugs and Biological Products	The Secretary may (by order in the form of a letter) require the holder of an approved drug application or biologics license to submit by a specified date the required assessments. [FDAAA 402(a); FFDCA 505B(b)(1); 21 USC 355c]	
		FDAAA specifies that the Secretary's letter requiring assessments of an approved drug must refer to a declined written request for pediatric exclusivity related studies (under FFDCA 505A) for a labeled indication and that the written request was not referred to the Foundation of the NIH for pediatric studies. It also expands "holder" to "sponsor or holder." [FDAAA 402(a); FFDCA 505B(b)(1); 21 USC 355c]
	To do so, the Secretary must find that: [FDAAA 402(a); FFDCA 505B(b)(1); 21 USC 355c]	
	(A) the drug or biological product is used for a substantial number of pediatric patients for the labeled indications; and the *absence* of adequate labeling could pose *significant risks* to pediatric patients;	(A) the drug or biological product is used for a substantial number of pediatric patients for the labeled indications; and the *presence* of adequate pediatric labeling "could confer a *benefit* on pediatric patients;" [FDAAA 402(a); FFDCA 505B(b)(1)(A); 21 USC 355c]
	or (B) there is reason to believe that the drug or biological product would represent a meaningful therapeutic benefit over existing therapies for pediatric patients for one or more of the claimed indications;	or (B) there is reason to believe that the drug or biological product would represent a meaningful therapeutic benefit over existing therapies for pediatric patients for one or more of the claimed indications; [FDAAA 402(a); FFDCA 505B(b)(1)(B); 21 USC 355c]
	and the *absence* of adequate labeling could pose *significant risks* to pediatric patients.	
	[Clause did not appear independently of the other two findings.]	or (C) the *absence* of adequate labeling could pose *a risk* to pediatric patients. [FDAAA authorizes the Secretary to act based on this independently of the previous two types of finding.] [FDAAA 402(a); FFDCA 505B(b)(1)(C); 21 USC 355c]

Topic	Previous Law	FDAAA Title IV
Deferrals	For a new drug or biological product, the Secretary may defer submission of some or all required assessments until a specified date after approval of the drug or issuance of the license for a biological product upon finding that the drug or biological product is ready for approval for use in adults before pediatric studies are complete; pediatric studies should be delayed until additional safety or effectiveness data have been collected; or there is another appropriate reason for deferral. The applicant must also submit to the Secretary certification of the grounds for deferring the assessments; a description of the planned or ongoing studies; and evidence that the studies are being conducted or will be conducted with due diligence and at the earliest possible time. [FDAAA 402(a); FFDCA 505B(a)(3); 21 USC 355c]	
	No provision.	An applicant must include a *timeline* for the completion of such studies. FDAAA requires an *annual review* of each approved deferral, for which the applicant must submit to the Secretary detailed information on its progress in conducting pediatric studies or, if no progress has been made, evidence of documentation that such studies will be conducted with due diligence and at the earliest possible time. It also requires that all information submitted as part of this annual review be promptly made available to the *public*, including through the FDA website. [FDAAA 402(a); FFDCA 505B(a)(3); 21 USC 355c]
Waivers	**Full waiver.** At the request of an applicant (or, for a new drug or biological product, on the initiative of the Secretary), the Secretary shall grant a full waiver, as appropriate, of the requirement to submit assessments under this subsection if the applicant certifies and the Secretary finds that (1) necessary studies are impossible or highly impracticable (because, for example, the number of patients in that age group is so small or patients in that age group are geographically dispersed); or (2) there is evidence strongly suggesting that the drug or biological product would be ineffective or unsafe in all pediatric age groups. [FDAAA 402(a); FFDCA 505B(a)(4)(A) and 505B(b)(2)(A); 21 USC 355c]	
	Partial waiver. At the request of an applicant (or, for a new drug or biological product, on the initiative of the Secretary), the Secretary shall grant a partial waiver, as appropriate, of the requirement to submit assessments under this subsection with respect to a specific pediatric age group if the applicant certifies and the Secretary finds that: (1) necessary studies are impossible or highly impracticable; (2) there is evidence strongly suggesting that the drug or biological product would be ineffective or unsafe in that age group; (3) the drug or biological product does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients in that age group, is not likely to be used in a substantial number of pediatric patients in that age group, and (for a marketed drug or biological product) the absence of adequate labeling could not pose significant risks to pediatric patients; or (4) the applicant can demonstrate that reasonable attempts to produce a pediatric formulation necessary for that age group have failed. [FDAAA 402(a); FFDCA 505B(a)(4)(B) and 505B(b)(2)(B); 21 USC 355c]	
	If a waiver is granted on the grounds that it is not possible to develop a pediatric formulation, the waiver shall cover only the pediatric groups requiring that formulation. [FDAAA 402(a); 505B(b)(2)(C); 21 USC 355c]	
		An applicant seeking a full or partial waiver must submit to the Secretary *documentation* detailing why a pediatric formulation cannot be developed. If a waiver is granted, the applicant's submission must promptly be made *public*, including through posting on the FDA website. [FDAAA 402(a); FFDCA 505B(a)(4)(C) and 505B(b)(2)(C); 21 USC 355c]
Labeling	If the Secretary grants a full or partial waiver because there is evidence that a drug or biological product would be ineffective or unsafe in pediatric populations, the information shall be included in the labeling for the drug or biological product. [FDAAA 402(a); FFDCA 505B(a)(4)(D) and 505B(b)(2)(D); 21 USC 355c]	

Topic	Previous Law	FDAAA Title IV
Relationship to Other Pediatric Provisions	To require a sponsor to submit a pediatric assessment of an approved drug or licensed biological product, the Secretary must have (1) issued a written request for a study, (2) received no agreement to the study from the drug's sponsor, and (3) certified that neither the program for pediatric studies of drugs (at NIH under PHSA 409I) or the Foundation for the NIH (FNIH, under PHSA 499) had sufficient funds to conduct the study, or certified in the Federal Register that no contract or grant had been awarded under those programs although funds were available. After determining that no holder will agree to the written request, the Secretary shall certify whether the Secretary has sufficient funds to conduct the study, taking into account the prioritization under PHSA 409I.	This paragraph regarding the Secretary's requiring the holder of a approved application for a drug or biological product to conduct pediatric studies no longer appears in FFDCA 505B. *[FDAAA (Title V) places an altered version in FFDCA 505A. If the holder declines a written request for a pediatric study and the Secretary continues to determine there is a need for such a study, the Secretary is now required to determine whether FNIH has sufficient funds (no mention is made of the NIH program for pediatric studies of drugs in this context). If funds are available, the Secretary must refer studies to FNIH and FNIH must fund them. If FNIH does not have sufficient funds, the Secretary may require that the holder of the approved application conduct the studies under PREA (FFDCA 505B). [FDAAA 502(a); FFDCA 505A(n)(1)(A); 21 USC 355a]]*
Disclosure of Confidential Information		Regarding requests for studies of approved products or the dissemination of pediatric information following a completed pediatric assessment, FDAAA states it does not alter or amend sections of U.S. Code titles regarding Food and Drugs, Government Organization and Employees, or Crimes and Criminal Procedure regarding the disclosure of confidential information. [FDAAA 402(a); FFDCA 505B(b)(3) and 505B(h)(3); 21 USC 355c]
Meaningful Therapeutic Benefit	The law defined "meaningful therapeutic benefit over existing therapies" as when: (1) the drug or biological product would represent a significant improvement in the treatment, diagnosis, or prevention of a disease, compared with marketed products adequately labeled for that use in the relevant pediatric population; or (2) the drug or biological product is in a class of products or for an indication for which there is a need for additional options. [FDAAA 402(a); FFDCA 505B(c); 21 USC 355c]	
	The law based the assessment on the Secretary's estimation.	FDAAA changes "the Secretary estimates" to "the Secretary determines." [FDAAA 402(a); FFDCA 505B(c); 21 USC 355c]
Misbranding	A drug or biological product may be considered misbranded and subject to relevant enforcement action solely for the failure to submit a required assessment or to request approval of a pediatric formulation in accordance with applicable provisions of this section. However, the law does not allow enforcement action under the penalty (imprisonment or fines) authority of this title; and does not allow the failure to submit the assessment or request to be the basis for a proceeding to withdraw approval for a drug or to revoke the license for a biological product. [FDAAA 402(a); FFDCA 505B(d); 21 USC 355c]	
Meeting with Sponsor	Requires that the Secretary, before and during the investigational process for a new drug or biological product, meet with the sponsor of the new drug or biological product to discuss information that the sponsor submits on plans and timelines for pediatric studies; or any planned request by the sponsor for waiver or deferral of pediatric studies. [FDAAA 402(a); FFDCA 505B(e); 21 USC 355c]	

Topic	Previous Law	FDAAA Title IV
Internal Committee	No provision.	The Secretary must establish an internal committee, composed of FDA employees with specified expertise, to participate in the review of pediatric plans, assessments, deferrals, and waivers. [FDAAA 403; FFDCA 505C; 21 USC 355d] (**Note:** This is the same internal committee to which FDAAA 502(a) [FFDCA 505A(f); 21 USC 355a] refers; see next section.) The Secretary must document the internal committee's activity, track pending assessments, and place the information on the FDA website for easy public access. The internal committee must conduct a retrospective review and analysis of assessments, deferrals, and waivers to the Secretary, who would be required to issue recommendations for improvements. [FDAAA 402(a); FFDCA 505B(f); 21 USC 355c]
Review of Pediatric Plans, Assessments, Deferrals, and Waivers	No provision.	The review must include analysis of the quality and consistency of pediatric information in pediatric assessments and the appropriateness of waivers and deferrals granted. The Secretary must, based on such review, issue recommendations to the review divisions for improvements and initiate guidance to industry. The Secretary must, in consultation with the internal committee, track and make available to the public specified statistics on the numbers of assessments, study designs, deferral and waiver requested and granted, pediatric formulations developed, labeling changes, etc. The report must include the reasons for each of those events not happening. [FDAAA 402(a); FFDCA 505B(f); 21 USC 355c]
Dispute Resolution	No provision.	FDAAA establishes a dispute resolution procedure for when a sponsor does not agree with the Commissioner's request for a label change. In those cases, it requires the Commissioner to refer the dispute to the Pediatric Advisory Committee for review and recommendation. If the sponsor continues to disagree with a requested labeling change, the Commissioner may deem the drug to be misbranded. The Commissioner must refer the dispute to the Pediatric Advisory Committee within 30 days of a sponsor's disagreeing to change the label. Nothing in this subsection shall preclude, delay, or serve as the basis to stay other courses of action via the Pediatric Advisory Committee process or an enforcement action under this Act. [FDAAA 402(a); FFDCA 505B(g)(1); 21 USC 355c]
Labeling to Include Secretary's Determination	No provision.	Upon making a determination that a pediatric assessment does or does not demonstrate that the subject drug is safe and effective in pediatric populations or subpopulations, including whether such assessment results are inconclusive, the Secretary must order the label to include information about those results and a statement of the Secretary's determination. [FDAAA 402(a); FFDCA 505B(g)(2); 21 USC 355c]

Topic	Previous Law	FDAAA Title IV
Dissemination of Pediatric Information	No provision.	The Secretary must make available to the public in an easily accessible manner, including by posting on the FDA website, the medical, statistical, and clinical pharmacology reviews of a submitted pediatric assessment. The Secretary must require the sponsor of an assessment that results in certain labeling changes to distribute such information to health care providers. [FDAAA 402(a); FFDCA 505B(h); 21 USC 355c]
Adverse Event Reporting	No provision.	Following a labeling change, the Secretary must refer all adverse event reports to the Office of Pediatric Therapeutics (OPT). For the first year after the change, the OPT director must provide for their review by the Pediatric Advisory Committee (PAC) and obtain its recommendations for action by the Secretary. In subsequent years, the OPT director may refer the adverse event reports to the PAC. FDAAA states that these requirements "shall supplement, not supplant, other review of such adverse event reports by the Secretary." [FDAAA 402(a); FFDCA 505B(i); 21 USC 355c]
Orphan Drugs	Unless the Secretary requires otherwise by regulation, this section does not apply to any drug for an indication for which orphan designation has been granted under this title. [FDAAA 402(a); FFDCA 505B(k); 21 USC 355c]	
Institute of Medicine Study	No provision.	FDAAA requires that the Secretary contract with the IOM to conduct a study and report to Congress regarding pediatric studies and resulting labeling changes. It directs that the IOM review and assess, using a representative sample of studies, the use of extrapolation, alternative endpoints, neonatal assessment tools, number and type of pediatric adverse events, and ethical issues in pediatric clinical trials. [FDAAA 402(a); FFDCA 505B(l); 21 USC 355c]
Government Accountability Office Report	No codified provision.	FDAAA requires a GAO report, in consultation with the Secretary, to Congress by January 1, 2011, that addresses the effectiveness of FFDCA 505A and 505B and PHSA 409I in ensuring that medicines used by children are tested and properly labeled. It specifies required elements of that report. FDAAA does not indicate that this provision be placed within the U.S. Code. [FDAAA 404; not in FFDCA or USC]
Reference to Sunset	The authority under this section shall remain in effect so long as an application subject to this section may be accepted for filing by the Secretary on or before the date specified in the market exclusivity for pediatric studies of drugs section of this title. [FDAAA 402(a); FFDCA 505B(m); 21 USC 355c]	

Title V. Best Pharmaceuticals for Children Act of 2007

Title V of FDAAA reauthorizes and changes legislation first passed in 1997. As part of the FDA Modernization Act of 1997 (P.L. 105-115), Congress provided drug manufacturers with a financial incentive to conduct pediatric use studies on their patented products. The "Pediatric Studies of Drugs" provision provided that 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.[18] This tool is the second approach that FDA and Congress have taken to encouraging pediatric drug research, the other, required pediatric assessments of new products, is discussed in the preceding section of this report regarding FDAAA Title IV.

> For further information, see CRS Report RL33986, *FDA's Authority to Ensure That Drugs Prescribed to Children Are Safe and Effective*, by Susan Thaul.

In 2002, the Best Pharmaceuticals for Children Act (BPCA 2002; P.L. 107-109) reauthorized the exclusivity provisions for another five years. It also added provisions to encourage pediatric research of products that were no longer covered by patent or other marketing exclusivity agreements, to which pediatric exclusivity was not relevant. It required the Secretary to list those *off-patent* products for which pediatric studies are needed to assess safety and effectiveness. It also established an off-patent research fund at NIH (PHSA 409I) and authorized appropriations of $200 million for FY2002 and such sums as are necessary for each of the five years until the provisions were set to sunset on October 1, 2007.

For *on-patent* drugs whose manufacturers declined FDA's written requests for studies (and, therefore, exclusivity), BPCA 2002 amended FFDCA 505A to allow FDA to refer drugs needing pediatric studies to the Foundation for the NIH (FNIH, PHSA 499), creating a second program of FDA-NIH collaboration.[19]

Other provisions in the 2002 BPCA included giving priority status to pediatric supplemental applications; the establishment of an FDA Office of Pediatric Therapeutics (OPT); the definition of pediatric age groups to include neonates; and a direction to the Secretary to contract with the IOM for a review of regulations, federally prepared or supported reports, and federally supported evidence-based research, all relating to clinical research involving children. The IOM report to Congress was also to include recommendations on best practices relating to research involving children.[20]

Title V of FDAAA again reauthorizes the pediatric exclusivity program, amending FFDCA 505A to sunset on October 1, 2012. It also encourages research on off-patent products, strengthens the

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

[19] The Foundation supports the research mission of NIH using public-private partnerships; see http://www.fnih.org/about.

[20] See IOM, *Ethical Conduct of Clinical Research Involving Children*, Committee on Clinical Research Involving Children (Washington, DC: National Academies Press, 2004), done with funding from NIH and FDA.

requirements for labeling changes based on the results of pediatric use studies, and provides for the reporting of adverse events.

FDAAA authorizes the Secretary to grant additional marketing exclusivity, for both new drugs and drugs already on the market, only after a sponsor has completed and reported on the studies that the Secretary has requested in writing, including appropriate formulations of the drug for each age group of interest, and after any appropriate labeling changes are approved, all within the agreed upon time frames. An applicant who turns down a request on the grounds that developing appropriate pediatric formulations of the drug is not possible must provide evidence to support that claim.

The new law requires that the sponsor propose pediatric labeling resulting from the studies. For a product studied under this section, the labeling must include study results and the Secretary's determination whether those results demonstrate the drug's safety and effectiveness (if the results do or do not indicate safety and effectiveness, or if they are inconclusive). The product sponsor must disseminate labeling change information to health care providers, and the Commissioner must report to the Secretary on the review of all adverse event reports and recommendations on actions in response. Other provisions of the law set time frames for the actions it requires.

Public notice requirements are expanded beyond the current notice of an exclusivity decision to include copies of the written request. The Secretary must also publicly identify any drug with a developed pediatric formulation that studies had demonstrated to be safe and effective for children that an applicant has not introduced onto the market within one year.

A new dispute resolution process includes referral to the Pediatric Advisory Committee. The internal review committee, which FDAAA Title IV requires the Secretary to establish, must review all written requests. The Secretary, with that committee, must track all pediatric studies and labeling changes according to specified questions.

Other provisions require applicants to submit, along with the report of requested studies, all postmarket adverse event reports regarding that drug; refine study scope to allow the Secretary to include preclinical studies; and except from exclusivity any drug with another exclusivity that is to expire in less than nine months.

FDAAA amends PHSA Section 409I (as discussed earlier), which required that the Secretary, through the NIH Director and in consultation with the Commissioner and pediatric research experts, list approved drugs for which pediatric studies are needed to assess safety and effectiveness. It changes the specifications from an annual list of approved drugs to a list, revised every three years, of priority study needs in pediatric therapeutics, including drugs or indications.

If the Secretary determines there is a need for pediatric information for a drug for which pediatric studies have not been completed, the Secretary must either issue a proposal to award a grant to conduct such studies, if funds are available through FNIH, or refer the drug for inclusion on the list established under PHSA Section 409I. FDAAA also requires reports from the IOM and the GAO.

The provisions in Title V of FDAAA make up the following two tables: the first addressing amendments to FFDCA, the second relating to PHSA.

Table 7. Comparison of *Best Pharmaceuticals for Children Act of 2007* *(FDAAA Title V, Section 502(a))* with Previous Law

Topic	Previous Law	FDAAA Title V, Section 502(a)
Definition of Studies	As used in this section, the term "pediatric studies" or "studies" means at least one clinical investigation (that, at the Secretary's discretion, may include pharmacokinetic studies) in pediatric age groups (including neonates in appropriate cases) in which a drug is anticipated to be used. [FDAAA 502(a); FFDCA 505A(a); 21 USC 355a]	
		Adds that, at the Secretary's discretion, clinical investigation may include preclinical studies. [FDAAA 502(a); FFDCA 505A(a); 21 USC 355a]
Market Exclusivity for New Drugs	Six-month pediatric exclusivity is granted if, prior to approval of an application that is submitted under section 355(b)(1) of this title, the Secretary determines that information relating to the use of a *new drug* in the pediatric population may produce health benefits in that population, the Secretary makes a written request for pediatric studies (which shall include a timeframe for completing such studies), and such studies are completed within any such timeframe and the reports thereof submitted in accordance with subsection (d)(2) of this section or accepted in accordance with subsection (d)(3) of this section. [FDAAA 502(a); FFDCA 505A(b); 21 USC 355a]	
		Adds that the applicant agrees to the request and that such studies are completed using appropriate formulations for each age group for which the study is requested. [FDAAA 502(a); FFDCA 505A(b)(1); 21 USC 355a]
Market Exclusivity for Already Marketed Drugs	Six-month pediatric exclusivity is granted if the Secretary determines that information relating to the use of an *approved drug* in the pediatric population may produce health benefits in that population and makes a written request to the holder of an approved application under section 355(b)(1) of this title for pediatric studies (which shall include a timeframe for completing such studies), the holder agrees to the request, the studies are completed within any such timeframe, and the reports thereof are submitted in accordance with subsection (d)(2) of this section or accepted in accordance with subsection (d)(3) of this section. [FDAAA 502(a); FFDCA 505A(c); 21 USC 355a]	
		Adds that such studies are completed using appropriate formulations for each age group for which the study is requested. [FDAAA 502(a); FFDCA 505A(c)(1); 21 USC 355a]
Extension of Exclusivity	Extended by six months other exclusivities granted (such as for new drugs, certain generic drugs, drugs for rare diseases or conditions) under the FFDCA. [FDAAA 502(a); FFDCA 505A(b)(1)(B) and 505A(c)(1)(B); 21 USC 355a]	
Exception	No provision.	Adds that the Secretary shall not extend the exclusivity period if the determination is made less than 9 months before the expiration of exclusivity period. [FDAAA 502(a); FFDCA 505A(b)(2) and 505A(c)(2); 21 USC 355a]

Topic	Previous Law	FDAAA Title V, Section 502(a)
Agreement for Studies	The Secretary may, pursuant to a written request and after consultation with the sponsor of an application for an investigational new drug or a new drug, or the holder of an approved application for a drug, agree with the sponsor or holder for the conduct of pediatric studies for such drug. Such agreement shall be in writing and shall include a timeframe for such studies. [FDAAA 502(a); FFDCA 505A(d)(1); 21 USC 355a]	
		Request for studies. Adds that a single written request may relate to more than one use of a drug; and may include uses that are both approved and unapproved. [FDAAA 502(a); FFDCA 505A(d)(1); 21 USC 355a] Combines language relating to new drugs and already approved drugs. Requires the applicant or holder to respond to the Secretary's written request within 180 days, indicating either when studies will be initiated or the reasons for declining the request. [FDAAA 502(a); FFDCA 505A(d)(2); 21 USC 355a]
	No provision.	An applicant or holder who does not agree with the request on the grounds that it is not possible to develop the appropriate pediatric formulation must submit to the Secretary the reasons such pediatric formulations cannot be developed. [FDAAA 502(a); FFDCA 505A(d)(2)(ii); 21 USC 355a]
	No provision.	An applicant or holder who agrees to the request for such studies shall provide the Secretary, at the same time as the submission of the reports of such studies, with all available postmarket adverse event reports regarding the subject drug. [FDAAA 502(a); FFDCA 505A(d)(2)(B); 21 USC 355a]
Representation of Minorities	The law directs the Secretary to take into account adequate representation of children of ethnic and racial minorities. [FDAAA 502(a); FFDCA 505A(d); 21 USC 355a]	
	The Secretary is required to do this in reaching an agreement regarding written protocols.	The Secretary is required to do this "[i]n issuing such a request." [FDAAA 502(a); FFDCA 505A(d)(1); 21 USC 355a]

Topic	Previous Law	FDAAA Title V, Section 502(a)
Determination by Secretary	The Secretary must determine if such studies were or were not conducted in accordance with the original written request and the written agreement and reported in accordance with the requirements of the Secretary for filing, and so notify the sponsor or holder within a specified number of days after the submission of the report of the studies. [FDAAA 502(a); FFDCA 505A(d)(3); 21 USC 355a]	
	If the sponsor or holder and the Secretary agree upon written protocols for the studies, the studies requirement is satisfied upon the completion of the studies and submission of the reports thereof in accordance with the original written request and the written agreement. For agreed upon studies, the Secretary was required to make the determination within 60 days of the report's submission. If the sponsor or holder and the Secretary had not agreed in writing on the protocols for the studies, the requirement for pediatric studies was satisfied when such studies had been completed and the reports accepted by the Secretary. The Secretary was required to accept or reject such reports and so notify the sponsor or holder not later than 90 days after the submission of the reports of the studies.	FDAAA requires that the Secretary make the determination within 180 days of the report's submission. [FDAAA 502(a); FFDCA 505A(d)(3); 21 USC 355a]
	The Secretary's only responsibility in accepting or rejecting the reports shall be to determine whether the studies fairly respond to the written request, have been conducted in accordance with commonly accepted scientific principles and protocols, and have been reported in accordance with the requirements of the Secretary for filing. [FDAAA 502(a); FFDCA 505A(d)(3); 21 USC 355a]	
Written Request to Holders of Approved Applications for Drugs that Have Market Exclusivity	If the Secretary makes a written request for pediatric studies (including neonates, as appropriate) under subsection (c) of this section to the holder of an approved new drug application, the holder, not later than 180 days after receiving the written request, shall respond to the Secretary as to the intention of the holder to act on the request by indicating when the pediatric studies will be initiated, if the holder agrees to the request; or indicating that the holder does not agree to the request.	Addresses requests for studies of both new drugs and already approved drugs together; see above.

Topic	Previous Law	FDAAA Title V, Section 502(a)
Referral if Pediatric Studies Not Completed: No Agreement to Request	The Secretary is required to act if the manufacturer does not agree to a written request within the specified time period, and if the Secretary determines that there is a continuing need for information relating to the use of the drug in the pediatric population (including neonates, as appropriate). [Previous law addressed this in FFDCA 505A(d)(4)(B); and FDAAA 502(a) places it in FFDCA 505A(n); 21 USC 355a]	
	The Secretary was to refer the drug to FNIH, established under 42 USC 290b, for the conduct of the pediatric studies described in the written request.	The Secretary must make the determination whether further study is needed through the internal committee established under FFDCA 505C. Different procedures are specified for drugs with and without current patents.
		For a drug with an unexpired patent, the Secretary must first certify whether FNIH has sufficient funding for the studies in the written request. -If funding is available, requires the Secretary to refer the written request to FNIH, and requires FNIH to fund the studies. -If funding is not available, the Secretary must consider whether to require pediatric assessments under FFDCA 505B(b). [FDAAA 502(a); FFDCA 505A(n)(1)(A); 21 USC 355a] For a drug with no current patent, requires that the Secretary refer the drug for inclusion on the list established under PHSA 409I. [FDAAA 502(a); FFDCA 505A(n)(1)(B); 21 USC 355a]
Public Notice	The Secretary shall give public notice of the name of the drug, the name of the manufacturer, and the indications to be studied made in a referral to the FNIH.	FDAAA deletes this provision and adds: For a drug for which the Secretary decides *not* to require an assessment under FFDCA 505B, the Secretary must give public notice and the basis for that decision. [FDAAA 502(a); FFDCA 505A(n)(2); 21 USC 355a]
Lack of Funds	On referral of a drug under subparagraph (B)(i), FNIH shall issue a proposal to award a grant to conduct the requested studies unless FNIH certifies to the Secretary, within a timeframe that the Secretary determines is appropriate through guidance, that FNIH does not have funds available under PHSA 499 to conduct the requested studies. If FNIH so certifies, the Secretary shall refer the drug for inclusion on the list established under PHSA 409I for the conduct of the studies.	The law was rewritten so that for a drug with an unexpired patent, the Secretary must certify whether the FNIH has sufficient funding to conduct the studies *before* referring a request to FNIH. [FDAAA 502(a); FFDCA 505A(n)(1)(A); 21 USC 355a] It requires the FNIH to fund a study that the Secretary does refer. [FDAAA 502(a); FFDCA 505A(n)(1)(A); 21 USC 355a].
No Requirement to Refer	Nothing in this subsection shall be construed to require that every declined written request shall be referred to FNIH.	No provision.

Topic	Previous Law	FDAAA Title V, Section 502(a)
Written Requests for New Drugs	For a drug for which a written request had not been accepted before marketing approval, if the Secretary determines that there is a continuing need for information relating to the use of the drug in the pediatric population (including neonates, as appropriate), the Secretary shall issue a written request after the date of approval of the drug. [FFDCA 505A(d)(4)(F)]	FDAAA changes how the Secretary would handle a declined request for studies. If a written request is not accepted by the sponsor or holder of an application, and the Secretary does not refer the request to FNIH (under FFDCA 505A(n)(1)(A)), the Secretary may require the holder to submit a pediatric assessment under FFDCA 505B(b)(1). [FDAAA 502(a); FFDCA 505A(n)(1)(A); 21 USC 355a]
Delay of Effective Date for Certain Application	The Secretary shall delay for up to 90 days the approval of a generic or other product whose application relies on safety and effectiveness studies conducted by an entity other than the applicant (such as for a new formulation (under FFDCA 505(b)(2)) or a generic version (under FFDCA 505(j)) until a determination is made regarding pediatric studies under this section (FFDCA 505A). In the event that requirements of this section are satisfied, the applicable six-month marketing exclusivity shall be deemed to have been running during the period of delay.	No provision.
Notice of Determinations on Studies Requirement	The Secretary shall publish a notice of any determination that the requirements for the conduct of pediatric studies have been met and that submissions and approvals under FFDCA 505(b)(2) or (j) [generic] for a drug will be subject to the provisions of this section. [FDAAA 502(a); FFDCA 505A(e)(1); 21 USC 355a]	
		Such notice must be published within 30 days of the Secretary's determination regarding market exclusivity and must include a copy of the written request under subsection (b) or (c). [FDAAA 502(a); FFDCA 505A(e)(1); 21 USC 355a]
	No provision.	The Secretary must publicly identify any drug with a developed pediatric formulation that studies have demonstrated to be safe and effective for children if its sponsor has not introduced the pediatric formulation onto the market within one year. [FDAAA 502(a); FFDCA 505A(e)(2); 21 USC 355a]
Internal Review of Written Requests and Pediatric Studies	No provision.	The internal review committee, which FDAAA 403 requires the Secretary to establish, must review all written requests. It may review studies submitted pursuant to this provision to make recommendations to the Secretary on whether to accept or reject the studies. The Secretary must, in consultation with the internal committee, track pediatric studies and labeling changes; and make available to the public specified information such as types of studies, and drugs and uses studied. [FDAAA 502(a); FFDCA 505A(f); 21 USC355a]

Topic	Previous Law	FDAAA Title V, Section 502(a)
Limitations	A drug to which the six-month period under subsection (b) or (c) of this section has already been applied (1) may receive an additional six-month period under subsection (c)(1)(A)(ii) of this section for a supplemental application if all other requirements under this section are satisfied, except that such a drug may not receive any additional such period under subsection (c)(2) of this section; and (2) may not receive any additional such period under subsection (c)(1)(B) of this section. [FDAAA 502(a); FFDCA 505A(g); 21 USC 355a]	
Relationship to Pediatric Research Requirements	Notwithstanding any other provision of law, if any pediatric study is required by a provision of law (including a regulation) other than this section and such study meets the completeness, timeliness, and other requirements of this section, such study shall be deemed to satisfy the requirement for market exclusivity pursuant to this section. [FDAAA 502(a); FFDCA 505A(h); 21 USC 355a]	
Priority Status for Labeling Changes	Any supplement to an application under FFDCA 505 proposing a labeling change pursuant to a report on a pediatric study under this section shall be considered to be a priority supplement; and shall be subject to the performance goals established by the Commissioner for priority drugs. [FDAAA 502(a); FFDCA 505A(i)(1); 21 USC 355a]	
		This provision now refers to pediatric applications and supplements. [FDAAA 502(a); FFDCA 505A(i)(1); 21 USC 355a]
Labeling Change Dispute Resolution	If, not later than 180 days after the date of submission of the application, the Commissioner determines that there is a disagreement with the sponsor on appropriate changes to the labeling for the drug that is the subject of the application, the Commissioner must request that the sponsor of the application make any labeling change that the Commissioner determines to be appropriate; and if the sponsor of the application does not agree to make a labeling change requested by the Commissioner, the Commissioner shall refer the matter to the Pediatric Advisory Committee. [FDAAA 502(a); FFDCA 505A(i)(2)(A); 21 USC 355a]	
	The law specified that the Commissioner determined that the related application was approvable and that the only open issue is the labeling change.	FDAAA refers to the Commissioner's determining that "the sponsor and the Commissioner have been unable to reach agreement." It also adds that the Commissioner must make the referral if the sponsor does not agree within 30 days of the request. [FDAAA 502(a); FFDCA 505A(i)(2)(A); 21 USC 355a]
	Not later than 90 days after receiving a referral, the Pediatric Advisory Committee shall review the pediatric study reports, and make a recommendation to the Commissioner concerning appropriate labeling changes, if any. The Commissioner shall consider the recommendations of the Pediatric Advisory Committee and, if appropriate, not later than 30 days after receiving the recommendation, make a request to the sponsor of the application to make any labeling change that the Commissioner determines to be appropriate. If the sponsor of the application, within 30 days after receiving a request, does not agree to make a labeling change requested by the Commissioner, the Commissioner may deem the drug that is the subject of the application to be misbranded. Nothing in this subsection limits the authority of the United States to bring an enforcement action under this chapter when a drug lacks appropriate pediatric labeling. Neither course of action (the Pediatric Advisory Committee process or an enforcement action referred to in the preceding sentence) shall preclude, delay, or serve as the basis to stay the other course of action. [FDAAA 502(a); FFDCA 505A(i)(2)(E); 21 USC 355a]	
Secretary's Determination Public	No provision.	The Secretary must, upon determining that a pediatric study conducted under this section does or does not demonstrate that the drug that is the subject of the study is safe and effective, including whether such study results are inconclusive, in pediatric populations or subpopulations, order the labeling of such product to include information about the results of the study and a statement of the Secretary's determination. [FDAAA 502(a); FFDCA 505A(j); 21 USC 355a]

Topic	Previous Law	FDAAA Title V, Section 502(a)
Dissemination of Pediatric Information	Not later than a specified number of days after the date of submission of a report on a pediatric study under this section, the Commissioner shall make available to the public a summary of the medical and clinical pharmacology reviews of pediatric studies conducted for the supplement, including by publication in the Federal Register. [FDAAA 502(a); FFDCA 505A(k)(1); 21 USC 355a]	
	The law allowed up to 180 days.	FDAAA allows up to 210 days. It also substitutes the Secretary for the Commissioner, adds statistical reviews, and refers to studies conducted under subsection (b) or (c). [FDAAA 502(a); FFDCA 505A(k)(1); 21 USC 355a] Requires, for studies that result in labeling changes reflected in the annual summary distribution, that their sponsors distribute, at least annually, such information to health care providers. [FDAAA 502(a); FFDCA 505A(k)(2); 21 USC 355a]
	Regarding dissemination of information of pediatric studies under this section, FDAAA states it does not alter or amend sections of U.S. Code titles regarding Food and Drugs, Government Organization and Employees, or Crimes and Criminal Procedure regarding the disclosure of confidential information. [FDAAA 502(a); FFDCA 505A was (j)(2), now (k)(3); 21 USC 355a]	
Adverse Event Reporting	No provision.	The Secretary must, for the year following a labeling change, ensure referral of all adverse event reports to the OPT, whose director must provide for their review by the Pediatric Advisory Committee and obtain its recommendations for action by the Secretary. In subsequent years, the Secretary must, as appropriate, refer all pediatric adverse event reports for a drug for which a pediatric study was conducted under this section to the OPT, whose director may refer them for review and recommendation to the Pediatric Advisory Committee. FDAAA states that these requirements "shall supplement, not supplant, other review of such adverse event reports by the Secretary." [FDAAA 502(a); FFDCA 505A(l); 21 USC 355a]
Interaction of Exclusivities	If the generic drug exclusivity period overlaps with the pediatric exclusivity period, the period will be extended by the number of days of the overlap. [FDAAA 502(a); FFDCA 505A(m); 21 USC 355a]	
Prompt Approval of Generic Drugs When Pediatric Information Is Added to Labeling	A drug for which an application has been submitted or approved under an abbreviated new drug application (ANDA, for a generic drug) shall not be considered ineligible for approval under that section or misbranded on the basis that the labeling of the drug omits a pediatric indication or any other aspect of labeling pertaining to pediatric use when the omitted indication or other aspect is protected by patent or by certain exclusivities. *Labeling.* The Secretary may require that the labeling of an approved generic drug (FFDCA 505(j)) that omits a pediatric indication or other required aspect of labeling include: a statement that the product is not labeled for all or specific pediatric uses because of marketing exclusivity held by another manufacturer; and a statement of any appropriate pediatric contraindications, warnings, or precautions that the Secretary considers necessary. FDAAA includes a clause to preserve pediatric exclusivity and other provisions under certain paragraphs of FFDCA 505, 505A, 505(j). [FDAAA 502(a); FFDCA 505A(o); 21 USC 355a]	

Topic	Previous Law	FDAAA Title V, Section 502(a)
Institute of Medicine Study	No provision.	The Secretary must contract, within 3 years of enactment, with the IOM to conduct a study and report to Congress regarding the written requests and studies conducted pursuant to this section. The IOM must review representative requests and studies since 1997 and labeling changes made as a result of such studies; assess the use of extrapolation, alternative endpoints, neonatal assessment tools, and ethical issues in pediatric clinical trials; and review and assess the pediatric studies of biological products; and make recommendations regarding appropriate incentives for encouraging pediatric studies of biologics. [FDAAA 502(a); FFDCA 505A(p); 21 USC 355a]
Secretary's Report to Congress	The Secretary was required to conduct a study of all relevant issues, as specified, and report to Congress, by January 1, 2001, based on the experience under the program established under this section.	No provision.
Sunset	The law provides a sunset date by which all written requests for pediatric studies must be made, applications accepted for filing, and all other requirements met to receive a 6-month marketing exclusivity under this section. [FDAAA 502(a); FFDCA 505A; 21 USC 355a]	
	The sunset date was October 1, 2007.	The sunset date is October 1, 2012. [FDAAA 502(a); FFDCA 505A(q); 21 USC 355a]

Table 8. Comparison of *Best Pharmaceuticals for Children Act of 2007* (*FDAAA Title V, Sections 502(b-f) and 503*) with Previous Law

Topic	Previous Law	FDAAA Title V, Sections 502(b-f) and 503
List of Priority Issues in Pediatric Therapeutics	The Secretary, acting through the NIH Director and in consultation with the Commissioner and experts in pediatric research, shall develop, prioritize, and publish an annual list of approved drugs needing additional studies of safety and effectiveness in the pediatric population.	The focus of the list is changed to "a priority list of needs in pediatric therapeutics, including drugs or indications that require study." The Secretary must develop and publish the list not later than one year after enactment, and revise it every three years. [FDAAA 502(b); PHSA 409I(a)(1); 42 USC 284m]
	The criteria for developing and prioritizing the list of drugs included available information, need for information, whether new pediatric studies concerning the drug may produce health benefits in the pediatric population; and whether reformulation of the drug is necessary.	The section refers to a list of needs, rather than a list of drugs. It also replaces the existing criteria with others that give examples within the categories of therapeutic gaps in pediatrics; particular pediatric diseases, disorders or conditions where more complete knowledge and testing of therapeutics may be beneficial in pediatric populations; and the adequacy of necessary infrastructure to conduct pediatric pharmacological research. [FDAAA 502(b); PHSA 409I(a)(2); 42 USC 284m]
Funding of Pediatric Studies and Research .	The Secretary shall award contracts to entities that have the expertise to conduct pediatric clinical trials (including qualified universities, hospitals, laboratories, contract research organizations, federally funded programs such as pediatric pharmacology research units, other public or private institutions, or individuals) to enable the entities to conduct pediatric studies concerning one or more drugs identified in the list. [FDAAA 502(b); PHSA 409I(b); 42 USC 284m]	
		The Secretary must act through NIH. The description of entities is expanded to include expertise with clinical trials "or other research"; and practice groups. In addition to contracts, the Secretary may use grants or other appropriate funding mechanisms. [FDAAA 502(b); PHSA 409I(b); 42 USC 284m]
Process for Proposed Pediatric Study Requests and Labeling Changes	No provision.	The NIH Director must submit, as appropriate, proposed pediatric study requests for consideration by the Commissioner for pediatric studies of a specific pediatric indication on the list of priority issues in pediatric therapeutics. The request must include the information required by FFDCA 505A requests. The NIH Director may submit a proposed pediatric study request for a drug for which there is an approved or submitted application under FFDCA Section 505(j); and there is no patent protection or market exclusivity protection for at least one form of the drug under the FFDCA; and additional studies are needed to assess the safety and effectiveness of the use of the drug in the pediatric population. [FDAAA 502(b); PHSA 409I(c)(1); 42 USC 284m]

Topic	Previous Law	FDAAA Title V, Sections 502(b-f) and 503
Written Request to Holders of Approved Applications for Drugs Lacking Exclusivity	The Commissioner, in consultation with the NIH Director, may issue a written request (which shall include a timeframe for negotiations for an agreement) for pediatric studies to all holders of an approved application for the drug under FFDCA 505 [21 USC 355]. Such a written request shall be made in a manner equivalent to the manner in which a written request is made under subsection (a) or (b) of FFDCA 505A [21 USC 355a], including with respect to information provided on the pediatric studies to be conducted pursuant to the request. [FDAAA 502(b); PHSA 409I(c)(2); 42 USC 284m]	
	The written request referred to a study of a drug identified in the list of drugs for which pediatric studies are needed.	The written request refers to a study of an indication or indications submitted pursuant to the list of priority issues in pediatric therapeutics. Studies must use appropriate formulations for each age group for which the study is requested. [FDAAA 502(b); PHSA 409I(c)(2); 42 USC 284m]
Requests for Contract Proposals	If the Commissioner does not receive a response to a written request within 30 days of the date on which a request was issued, or if a referral is made, the Secretary, acting through the NIH Director and in consultation with the Commissioner, shall publish a request for contract proposals to conduct the pediatric studies described in the written request. [FDAAA 502(b); PHSA 409I(c)(3); 42 USC 284m]	
		The Secretary must publish the request if the Commissioner has not received a response to a written request within 30 days. [FDAAA 502(b); PHSA 409I(c)(3); 42 USC 284m]
Disqualification	A holder that receives a first right of refusal shall not be entitled to respond to a request for contract proposals. [FDAAA 502(b); PHSA 409I(c)(4); 42 USC 284m]	
Guidance	Not later than 270 days after January 4, 2002, the Commissioner shall promulgate guidance to establish the process for the submission of responses to written requests.	No provision.
Funding	A contract under this section may be awarded only if a proposal for the contract is submitted to the Secretary in such form and manner, and containing such agreements, assurances, and information as the Secretary determines to be necessary to carry out this section. [FDAAA 502(b); PHSA 409I(c)(5); 42 USC 284m]	
		The Secretary may allow grants or other funding in addition to contracts. [FDAAA 502(b); PHSA 409I(c)(5); 42 USC 284m]
Reporting of Studies	On completion of a pediatric study in accordance with a contract awarded under this section, a report concerning the study shall be submitted to the NIH Director and the Commissioner. The report shall include all data generated in connection with the study. [FDAAA 502(b); PHSA 409I(c)(6)(A); 42 USC 284m]	
		The section refers to "an award" rather than "a contract." It also requires that the report include the written request. [FDAAA 502(b); PHSA 409I(c)(6)(A); 42 USC 284m]
Availability of Reports	Each report submitted shall be considered to be in the public domain (subject to FFDCA 505A(d)(4)(D) [21 USC 355a (d)(4)(D)]) and shall be assigned a docket number by the Commissioner. An interested person may submit written comments concerning such pediatric studies to the Commissioner, and the written comments shall become part of the docket file with respect to each of the drugs.	

Topic	Previous Law	FDAAA Title V, Sections 502(b-f) and 503
Action by Commissioner	The Commissioner shall take appropriate action in response to the reports. [FDAAA 502(b); PHSA 409I(c)(6)(B,C); 42 USC 284m]	
Requests for Labeling Change	During the 180-day period after the date on which a report is submitted, the Commissioner must review the report and such other data as are available concerning the safe and effective use in the pediatric population of the drug studied; and negotiate with the holders of approved applications for the drug studied for any labeling changes that the Commissioner determines to be appropriate and requests the holders to make. The Commissioner must place in the public docket file a copy of the report and of any requested labeling changes; and publish in the Federal Register a summary of the report and a copy of any requested labeling changes. [FDAAA 502(b); PHSA 409I(c)(7)(A,B,C); 42 USC 284m]	
		The Commissioner must also post information on the FDA website. [FDAAA 502(b); PHSA 409I(c)(7)(C); 42 USC 284m]
Dispute Resolution	If, not later than the end of the 180-day period specified, the holder of an approved application for the drug involved does not agree to any labeling change requested by the Commissioner under that paragraph, the Commissioner shall refer the request to the Pediatric Advisory Committee. Not later than 90 days after receiving a referral, the Pediatric Advisory Committee shall review the available information on the safe and effective use of the drug in the pediatric population, including study reports submitted under this section, and make a recommendation to the Commissioner as to appropriate labeling changes, if any. Not later than 30 days after receiving a recommendation from the Pediatric Advisory Committee, the Commissioner shall consider the recommendation and, if appropriate, make a request to the holders of approved applications for the drug to make any labeling change that the Commissioner determines to be appropriate. If a holder of an approved application for a drug, within 30 days after receiving a request to make a labeling change, does not agree to make a requested labeling change, the Commissioner may deem the drug to be misbranded under FFDCA. [FDAAA 502(b); PHSA 409I(c); 42 USC 284m]	
	Nothing in this subsection limits the authority of the United States to bring an enforcement action under the Federal Food, Drug, and Cosmetic Act [21 USC 301 et seq.] when a drug lacks appropriate pediatric labeling. Neither course of action (the Pediatric Advisory Committee process or an enforcement action referred to in the preceding sentence) shall preclude, delay, or serve as the basis to stay the other course of action. [FDAAA 502(b); PHSA 409I(c)(11); 42 USC 284m]	
Recommendation for Formulation Changes	If a pediatric study completed under public contract indicates that a formulation change is necessary and the Secretary agrees, the Secretary shall send a nonbinding letter of recommendation regarding that change to each holder of an approved application.	The FDAAA-amended PHSA 409I(c) does not include this provision, which had been PHSA 409I(c)(12).
Dissemination of Pediatric Information	No provision.	Requires that the Secretary, acting through the NIH Director and within one year of enactment, study and report to Congress on the feasibility of establishing a compilation of information on pediatric drug use. [FDAAA 502(b); PHSA 409I(d); 42 USC 284m]
Authorization of Appropriations	There are authorized to be appropriated to carry out this section $200 million for the first year; and such sums as are necessary for each of the succeeding fiscal years. Any amount appropriated shall remain available to carry out this section until expended. [FDAAA 502(b); PHSA 409I(e)(1); 42 USC 284m]	
	FY2002 was specified as the first year and reference was made to five succeeding years.	FY2008 is specified as the first year and the section refers to four succeeding years. [FDAAA 502(b); PHSA 409I(e)(1); 42 USC 284m]

Topic	Previous Law	FDAAA Title V, Sections 502(b-f) and 503
Foundation for the National Institutes of Health (FNIH)	The law continues to require the Secretary, acting through the Director of NIH, to establish a nonprofit corporation to be known as the Foundation for the NIH, which shall not be an agency or instrumentality of the U.S. Government. FNIH is to support the NIH in its mission (*including collection of funds for pediatric pharmacologic research*), and to advance collaboration with biomedical researchers from universities, industry, and nonprofit organizations. FNIH may solicit and accept gifts, grants, and other donations, establish accounts, and invest and expend funds in support of various education and research programs, including a program to collect funds for certain pediatric pharmacologic research and studies. The law includes requirements regarding a board of directors, corporate and financial organization and reporting, service of federal employees, intellectual property rights, dissemination of scientific results by grantees and FNIH. FNIH may transfer funds to the NIH and any funds transferred under this paragraph shall be subject to all federal limitations relating to federally-funded research. The law authorizes to be appropriated for FNIH an aggregate $500,000 for each fiscal year. [PHSA 499(c)(1)(C); 42 USC 290b(c)(1)(C)]	
	The FNIH provision related to drugs that the Secretary had referred for listing as needing pediatric studies. These included drugs with an approved or submitted application under FFDCA 505(j) [generic drugs], drugs *without* patent protection or marketing exclusivity, or drugs *with* patent protection whose sponsors declined the Secretary's requests for study. FNIH was to issue a proposal to award a grant to conduct such studies unless FNIH certified to the Secretary that FNIH did not have available funds, in which case the Secretary was required to refer the drug for inclusion on the list established under PHSA 409I. [PHSA 499(c)(1)(C) referred to PHSA 409I(a)(1)(A) and FFDCA 505A(d)(4)(C), each of which FDAAA has amended as well.]	Regarding a drug with an *unexpired patent* for which the Secretary requested pediatric pharmacologic research and studies that the sponsor declined, the Secretary must *first* determine whether FNIH has sufficient funds to initiate and fund in its entirety. If there are sufficient funds, the Secretary must *then* refer the study to the FNIH. If there are insufficient funds, the Secretary must consider whether to require the pediatric assessments under FFDCA 505B(b) (PREA). [FDAAA 502(c); PHSA 499(c)(1)(C); 42 USC 290b(c)(1)(C)]
Advisory Committee on Pediatric Pharmacology	The law continues to require that the Secretary convene and consult an advisory committee on pediatric pharmacology. It specifies the committee composition, and requires that the committee advise and make recommendations to the Secretary, through the Commissioner and in consultation with the NIH Director, on matters relating to pediatric pharmacology. Specifies that the matters include pediatric research; identification of research priorities related to pediatric pharmacology and the need for additional treatments of specific pediatric diseases or conditions; and the ethics, design, and analysis of clinical trials related to pediatric pharmacology. [Section 14 of the Best Pharmaceuticals for Children Act; 42 USC 284m note]	
		FDAAA extends the advisory committee for another five years. [FDAAA 502(d); Section 14 of the Best Pharmaceuticals for Children Act; 42 USC 284m note]

Topic	Previous Law	FDAAA Title V, Sections 502(b-f) and 503
Pediatric Subcommittee of the Oncologic Drugs Advisory Committee	The law continues the Pediatric Subcommittee of the Oncologic Drugs Advisory Committee. [Section 15 of the Best Pharmaceuticals for Children Act; 42 USC 284m note]	
		FDAAA requires that the Subcommittee provide recommendations to the internal review committee created under FFDCA 505B(f) regarding implementation of the Pediatric Research Equity Amendments and the Best Pharmaceuticals for Children amendments to FFDCA sections 505A and 505B with respect to the treatment of pediatric cancers. FDAAA also extends operations of the subcommittee for five years; and updates, to January 31, 2009, the requirement for the Secretary's report to congressional committees on patient access to new therapeutic agents for pediatric cancer, including access to single patient use of new therapeutic agents. [FDAAA 502(e); Section 15 of the Best Pharmaceuticals for Children Act; 42 USC 284m note]
Toll-Free Number for Consumer Reports of Adverse Events	This provision is not in previous law; it refers to a proposed rule (69 FR 21778, April 22, 2004).	Requires that the rule proposed by the Commissioner on April 22, 2004, take effect on January 1, 2008, unless the Commissioner issues the final rule before that date. Excluded from the rule's application are a drug approved under FFDCA Section 505, a nonprescription drug, and a drug whose packaging includes a toll-free number with which to report adverse events to the manufacturer or distributor. [FDAAA 502(f)]
Investment in Tomorrow's Pediatric Researchers	In order to ensure the future supply of researchers dedicated to the care and research needs of children, the Director of the Institute, after consultation with the Administrator of the Health Resources and Services Administration, shall support activities to provide for: an increase in the number and size of institutional training grants to institutions supporting pediatric training; and an increase in the number of career development awards for health professionals who intend to build careers in pediatric basic and clinical research. [PHSA 452G(2); 42 USC 285g-10(a)(2)]	
		FDAAA inserts " ... , including pediatric pharmacological research." [FDAAA 503(a); PHSA 452G(2); 42 USC 285g-10(a)(2)]
	The law authorized to be appropriated such sums as may be necessary for each of FY2001 through FY2005.	FDAAA does not have an authorization of appropriations provision for this subsection.
Loan Repayment for Pediatric Research	The law authorizes the Secretary, in consultation with the Director of NIH, to establish a pediatric research loan repayment program. Through such program, the Secretary shall enter into contracts with qualified health professionals who agree to conduct pediatric research, in exchange for the Federal Government repayment of certain principal and interest of the educational loans of such professionals. The law also addresses reimbursements for tax liability; and the application of other loan repayment provisions. [PHSA 487F(a)(1); 42 USC 288-6(a)(1)]	
		FDAAA inserts after "pediatric research": "including pediatric pharmacological research." [FDAAA 503(b); PHSA 487F(a)(1); 42 USC 288-6(a)(1)]