

Pediatric Drug and Device Law Compilation

The Best Pharmaceuticals for Children Act, the Pediatric Research Equity Act, and the Pediatric Medical Device Safety and Improvement Act
As Amended by the Food and Drug Administration Safety and Innovation Act
July 2012

American Academy of Pediatrics
DEDICATED TO THE HEALTH OF ALL CHILDREN™



Best Pharmaceuticals for Children Act: Pediatric Exclusivity *Sec. 505A of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355a]*

SEC. 505A. [355a] PEDIATRIC STUDIES OF DRUGS.

(a) DEFINITIONS.—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, and, at the discretion of the Secretary, may include preclinical studies.

(b) MARKET EXCLUSIVITY FOR NEW DRUGS.—

(1) IN GENERAL.—Except as provided in paragraph (2), if, prior to approval of an application that is submitted under section 505(b)(1), 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), the applicant agrees to the request, such studies are completed using appropriate formulations for each age group for which the study is requested within any such timeframe, and the reports thereof are submitted and accepted in accordance with subsection (d)(3)—

(A)

(i)

(I) the period referred to in subsection (c)(3)(E)(ii) of section 505, and in subsection (j)(5)(F)(ii) of such section, is deemed to be five years and six months rather than five years, and the references in subsections (c)(3)(E)(ii) and (j)(5)(F)(ii) of such section to four years, to forty-eight months, and to seven and one-half years are deemed to be four and one-half years, fifty-four months, and eight years, respectively; or

(II) the period referred to in clauses (iii) and (iv) of subsection (c)(3)(E) of such section, and in clauses (iii) and (iv) of subsection (j)(5)(F) of such section, is deemed to be three years and six months rather than three years; and

(ii) if the drug is designated under section 526 for a rare disease or condition, the period referred to in section 527(a) is deemed to be seven years and six months rather than seven years; and

(B)

(i) if the drug is the subject of—

(I) a listed patent for which a certification has been submitted under subsection (b)(2)(A)(ii) or (j)(2)(A)(vii)(II) of section 505 and for which pediatric studies were submitted prior to the expiration of the patent (including any patent extensions); or

(II) a listed patent for which a certification has been submitted under subsections (b)(2)(A)(iii) or (j)(2)(A)(vii)(III) of section 505,

the period during which an application may not be approved under section 505(c)(3) or section 505(j)(5)(B) shall be extended by a period of six months after the date the patent expires (including any patent extensions); or

(ii) if the drug is the subject of a listed patent for which a certification has been submitted under subsection (b)(2)(A)(iv) or (j)(2)(A)(vii)(IV) of section 505, and in the patent infringement litigation resulting from the certification the court determines that the patent is valid and would be infringed, the period during which an application may not be approved under section 505(c)(3) or section 505(j)(5)(B) shall be extended by a period of six months after the date the patent expires (including any patent extensions).

(2) EXCEPTION.—The Secretary shall not extend the period referred to in paragraph (1)(A) or (1)(B) if the determination made under subsection (d)(3) is made later than 9 months prior to the expiration of such period.

(c) MARKET EXCLUSIVITY FOR ALREADY-MARKETED DRUGS.—

(1) IN GENERAL.—Except as provided in paragraph (2), 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 505(b)(1) for pediatric studies (which shall include a timeframe for completing such studies), the holder agrees to the request, such studies are completed using appropriate formulations for each age group for which the study is requested within any such timeframe, and the reports thereof are submitted and accepted in accordance with subsection (d)(3)—

(A)

(i)

(I) the period referred to in subsection (c)(3)(E)(ii) of section 505, and in subsection (j)(5)(F)(ii) of such section, is deemed to be five years and six months rather than five years, and the references in subsections (c)(3)(E)(ii) and (j)(5)(F)(ii) of such section to four years, to forty-eight months, and to seven and one-half years are deemed to be four and one-half years, fifty-four months, and eight years, respectively; or

(II) the period referred to in clauses (iii) and (iv) of subsection (c)(3)(D) of such section, and in clauses (iii) and (iv) of subsection (j)(5)(F) of such section, is deemed to be three years and six months rather than three years; and

(ii) if the drug is designated under section 526 for a rare disease or condition, the period referred to in section 527(a) is deemed to be seven years and six months rather than seven years; and

(B)

(i) if the drug is the subject of—

(I) a listed patent for which a certification has been submitted under subsection (b)(2)(A)(ii) or (j)(2)(A)(vii)(II) of section 505 and for which pediatric studies were submitted prior to the expiration of the patent (including any patent extensions); or

(II) a listed patent for which a certification has been submitted under subsection (b)(2)(A)(iii) or (j)(2)(A)(vii)(III) of section 505,

the period during which an application may not be approved under section 505(c)(3) or section 505(j)(5)(B)(ii) shall be extended by a period of six months after the date the patent expires (including any patent extensions); or

(ii) if the drug is the subject of a listed patent for which a certification has been submitted under subsection (b)(2)(A)(iv) or (j)(2)(A)(vii)(IV) of section 505, and in the patent infringement litigation resulting from the certification the court determines that the patent is valid and would be infringed, the period during which an application may not be approved under section 505(c)(3) or section 505(j)(5)(B) shall be extended by a period of six months after the date the patent expires (including any patent extensions).

(2) EXCEPTION.—The Secretary shall not extend the period referred to in paragraph (1)(A) or (1)(B) if the determination made under subsection (d)(3) is made later than 9 months prior to the expiration of such period.

(d) CONDUCT OF PEDIATRIC STUDIES.—

(1) REQUEST FOR STUDIES.—

(A) IN GENERAL.—The Secretary may, after consultation with the sponsor of an application for an investigational new drug under section 505(i), the sponsor of an application for a new drug under section 505(b)(1), or the holder of an approved application for a drug under section 505(b)(1), issue to the sponsor or holder a written request for the conduct of pediatric studies for such drug. In issuing such request, the Secretary shall take into account adequate representation of children of ethnic and racial minorities. Such request to conduct pediatric studies shall be in writing and shall include a timeframe for such studies and a request to the sponsor or holder to propose pediatric labeling resulting from such studies. If a request under this subparagraph does not request studies in neonates, such request shall include a statement describing the rationale for not requesting studies in neonates.

(B) SINGLE WRITTEN REQUEST.—A single written request—

(i) may relate to more than one use of a drug; and

(ii) may include uses that are both approved and unapproved.

(2) WRITTEN REQUEST FOR PEDIATRIC STUDIES.—

(A) REQUEST AND RESPONSE.—

(i) IN GENERAL.—If the Secretary makes a written request for pediatric studies (including neonates, as appropriate) under subsection (b) or (c), the applicant or holder, not later than 180 days after receiving the written request, shall respond to the Secretary as to the intention of the applicant or holder to act on the request by—

(I) indicating when the pediatric studies will be initiated, if the applicant or holder agrees to the request; or

(II) indicating that the applicant or holder does not agree to the request and stating the reasons for declining the request.

(ii) DISAGREE WITH REQUEST.—If, on or after the date of enactment of the Best Pharmaceuticals for Children Act of 2007, the applicant or holder does not agree to the request on the grounds that it is not possible to develop the appropriate pediatric formulation, the applicant or holder shall submit to the Secretary the reasons such pediatric formulation cannot be developed.

(B) ADVERSE EVENT REPORTS.—An applicant or holder that, on or after the date of enactment of the Best Pharmaceuticals for Children Act of 2007, 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 postmarket adverse event reports regarding the drug that is the subject of such studies and are available prior to submission of such reports.

(3) MEETING THE STUDIES REQUIREMENT.—Not later than 180 days after the submission of the reports of the studies, the Secretary shall accept or reject such reports and so notify the sponsor or holder. The Secretary's only responsibility in accepting or rejecting the reports shall be to determine, within the 180-day period, 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.

(4) EFFECT OF SUBSECTION.—Nothing in this subsection alters or amends section 301(j) of this Act or section 552 of title 5 or section 1905 of title 18, United States Code.

(e) NOTICE OF DETERMINATIONS ON STUDIES REQUIREMENT.—

(1) IN GENERAL.—The Secretary shall publish a notice of any determination, made on or after the date of enactment of the Best Pharmaceuticals for Children Act of 2007, that the requirements of subsection (d) have been met and that submissions and approvals under subsection (b)(2) or (j) of section 505 for a drug will be subject to the provisions of this section. Such notice shall be published not later than 30 days after the date of the Secretary's determination regarding market exclusivity and shall include a copy of the written request made under subsection (b) or (c).

(2) IDENTIFICATION OF CERTAIN DRUGS.—The Secretary shall publish a notice identifying any drug for which, on or after the date of enactment of the Best Pharmaceuticals for Children Act of 2007, a pediatric formulation was developed, studied, and found to be safe and effective in the pediatric population (or specified subpopulation) if the pediatric formulation for such drug is not introduced onto the market within one year after the date that the Secretary publishes the notice described in paragraph (1). Such notice identifying such drug shall be published not later than 30 days after the date of the expiration of such one year period.

(f) INTERNAL REVIEW OF WRITTEN REQUESTS AND PEDIATRIC STUDIES.—

(1) INTERNAL REVIEW.—The Secretary shall utilize the internal review committee established under section 505C to review all written requests issued on or after the date of enactment of the Best Pharmaceuticals for Children Act of 2007, in accordance with paragraph (2).

(2) REVIEW OF WRITTEN REQUESTS.—The committee referred to in paragraph (1) shall review all written requests issued pursuant to this section prior to being issued.

(3) REVIEW OF PEDIATRIC STUDIES.—The committee referred to in paragraph (1) may review studies conducted pursuant to this section to make a recommendation to the Secretary whether to accept or reject such reports under subsection (d)(3).

(4) ACTIVITY BY COMMITTEE.—The committee referred to in paragraph (1) may operate using appropriate members of such committee and need not convene all members of the committee.

(5) DOCUMENTATION OF COMMITTEE ACTION.—For each drug, the committee referred to in paragraph (1) shall document, for each activity described in paragraph (2) or (3), which members of the committee participated in such activity.

(6) TRACKING PEDIATRIC STUDIES AND LABELING CHANGES.—The Secretary, in consultation with the committee referred to in paragraph (1), shall track and make available to the public, in an easily accessible manner, including through posting on the Web site of the Food and Drug Administration—

(A) the number of studies conducted under this section and under section 409I of the Public Health Service Act;

(B) the specific drugs and drug uses, including labeled and off-labeled indications, studied under such sections;

(C) the types of studies conducted under such sections, including trial design, the number of pediatric patients studied, and the number of centers and countries involved;

(D) the number of pediatric formulations developed and the number of pediatric formulations not developed and the reasons such

formulations were not developed;

(E) the labeling changes made as a result of studies conducted under such sections;

(F) an annual summary of labeling changes made as a result of studies conducted under such sections for distribution pursuant to subsection (k)(2); and

(G) information regarding reports submitted on or after the date of enactment of the Best Pharmaceuticals for Children Act of 2007.

(g) LIMITATIONS.—Notwithstanding subsection (c)(2), a drug to which the six-month period under subsection (b) or (c) has already been applied—

(1) may receive an additional six-month period under subsection (c)(1)(A)(i)(II) for a supplemental application if all other requirements under this section are satisfied, except that such drug may not receive any additional such period under subsection (c)(1)(B); and

(2) may not receive any additional such period under subsection (c)(1)(A)(ii).

(h) RELATIONSHIP TO PEDIATRIC RESEARCH REQUIREMENTS.— Exclusivity under this section shall only be granted for the completion of a study or studies that are the subject of a written request and for which reports are submitted and accepted in accordance with subsection (d)(3). Written requests under this section may consist of a study or studies required under section 505B.

(i) LABELING CHANGES.—

(1) PRIORITY STATUS FOR PEDIATRIC APPLICATIONS AND SUPPLEMENTS.—Any application or supplement to an application under section 505 proposing a labeling change as a result of any pediatric study conducted pursuant to this section—

(A) shall be considered to be a priority application or supplement; and

(B) shall be subject to the performance goals established by the Commissioner for priority drugs.

(2) DISPUTE RESOLUTION.—

(A) REQUEST FOR LABELING CHANGE AND FAILURE TO AGREE.—If, on or after the date of enactment of the Best Pharmaceuticals for Children Act of 2007, the Commissioner determines that the sponsor and the Commissioner have been unable to reach agreement on appropriate changes to the labeling for the drug that is the subject of the application, not later than 180 days after the date of submission of the application—

(i) the Commissioner shall request that the sponsor of the application make any labeling change that the Commissioner determines to be appropriate; and

(ii) if the sponsor of the application does not agree within 30 days after the Commissioner's request to make a labeling change requested by the Commissioner, the Commissioner shall refer the matter to the Pediatric Advisory Committee.

(B) ACTION BY THE PEDIATRIC ADVISORY COMMITTEE.—Not later than 90 days after receiving a referral under subparagraph (A)(ii), the Pediatric Advisory Committee shall—

(i) review the pediatric study reports; and

(ii) make a recommendation to the Commissioner concerning appropriate labeling changes, if any.

(C) CONSIDERATION OF RECOMMENDATIONS.—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.

(D) MISBRANDING.—If the sponsor of the application, within 30 days after receiving a request under subparagraph (C), 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.

(E) NO EFFECT ON AUTHORITY.—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.

(j) OTHER LABELING CHANGES.—If, on or after the date of enactment of the Best Pharmaceuticals for Children Act of 2007, the Secretary determines 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, the Secretary shall order the labeling of such product to include information about the results of the study and a statement of the Secretary's determination.

(k) DISSEMINATION OF PEDIATRIC INFORMATION.—

(1) IN GENERAL.—Not later than 210 days after the date of submission of a report on a pediatric study under this section, the Secretary shall make available to the public the medical, statistical, and clinical pharmacology reviews of pediatric studies conducted under subsection (b) or (c).

(2) DISSEMINATION OF INFORMATION REGARDING LABELING CHANGES.—Beginning on the date of enactment of the Best Pharmaceuticals for Children Act of 2007, the Secretary shall include as a requirement of a written request that the sponsors of the studies that result in labeling changes that are reflected in the annual summary developed pursuant to subsection (f)(6)(F) distribute, at least annually (or more frequently if the Secretary determines that it would be beneficial to the public health), such information to physicians and other health care providers.

(3) EFFECT OF SUBSECTION.— Nothing in this subsection alters or amends section 301(j) of this Act or section 552 of title 5 or section 1905 of title 18, United States Code.

(l) ADVERSE EVENT REPORTING.—

(1) REPORTING IN FIRST 18-MONTH PERIOD.—Beginning on the date of enactment of the Best Pharmaceuticals for Children Act of 2007, during the 18-month period beginning on the date a labeling change is approved pursuant to subsection (i), the Secretary shall ensure that all adverse event reports that have been received for such drug (regardless of when such report was received) are referred to the Office of Pediatric Therapeutics established under section 6 of the Best Pharmaceuticals for Children Act (Public Law 107-109). In considering the reports, the Director of such Office shall provide for the review of the reports by the Pediatric Advisory Committee, including obtaining any recommendations of such Committee regarding whether the Secretary should take action under this chapter in response to such reports.

(2) REPORTING IN SUBSEQUENT PERIODS.—Following the 18-month period described in paragraph (1), the Secretary shall, as appropriate, refer to the Office of Pediatric Therapeutics all pediatric adverse event reports for a drug for which a pediatric study was conducted under this section. In considering such reports, the Director of such Office may provide for the review of such reports by the Pediatric Advisory Committee, including obtaining any recommendation of such Committee regarding whether the Secretary should take action in response to such reports.

(3) PRESERVATION OF AUTHORITY.—Nothing in this subsection shall prohibit the Office of Pediatric Therapeutics from providing for the review of adverse event reports by the Pediatric Advisory Committee prior to the 18-month period referred to in paragraph (1), if such review is necessary to ensure safe use of a drug in a pediatric population.

(4) EFFECT.—The requirements of this subsection shall supplement, not supplant, other review of such adverse event reports by the Secretary.

(m) CLARIFICATION OF INTERACTION OF MARKET EXCLUSIVITY UNDER THIS SECTION AND MARKET EXCLUSIVITY AWARDED TO AN APPLICANT FOR APPROVAL OF A DRUG UNDER SECTION 505(j).—If a 180-day period under section 505(j)(5)(B)(iv) overlaps with a 6-month exclusivity period under this section, so that the applicant for approval of a drug under section 505(j) entitled to the 180-day period under that section loses a portion of the 180-day period to which the applicant is entitled for the drug, the 180-day period shall be extended from—

(1) the date on which the 180-day period would have expired by the number of days of the overlap, if the 180-day period would, but for the application of this subsection, expire after the 6-month exclusivity period; or

(2) the date on which the 6-month exclusivity period expires, by the number of days of the overlap if the 180-day period would, but for the application of this subsection, expire during the six-month exclusivity period.

(n) REFERRAL IF PEDIATRIC STUDIES NOT SUBMITTED.—

(1) IN GENERAL.—Beginning on the date of enactment of the Best Pharmaceuticals for Children Act of 2007, if pediatric studies of a drug have not been submitted by the date specified in the written request issued or if the applicant or holder does not agree to the request under subsection (d) and if the Secretary, through the committee established under section 505C, 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 carry out the following:

(A) For a drug for which a listed patent has not expired, or for which a period of exclusivity eligible for extension under subsection (b)(1) or (c)(1) of this section or under subsection (m)(2) or (m)(3) of section 351 of the Public Health Service Act has not ended, make a determination regarding whether an assessment shall be required to be submitted under section 505B(b).

(B) For a drug that has no unexpired listed patents and for which no unexpired periods of exclusivity eligible for extension under subsection (b)(1) or (c)(1) of this section or under subsection (m)(2) or (m)(3) of section 351 of the Public Health Service Act apply, the Secretary shall refer the drug for inclusion on the list established under section 409I of the Public Health Service Act for the conduct of studies.

(2) PUBLIC NOTICE.—The Secretary shall give the public notice of a decision under paragraph (1)(A) not to require an assessment under section 505B and the basis for such decision.

(3) EFFECT OF SUBSECTION.—Nothing in this subsection alters or amends section 301(j) or section 552 of title 5 or section 1905 of title 18, United States Code.

(o) PROMPT APPROVAL OF DRUGS UNDER SECTION 505(J) WHEN PEDIATRIC INFORMATION IS ADDED TO LABELING.—

(1) GENERAL RULE.—A drug for which an application has been submitted or approved under section 505(j) shall not be considered ineligible for approval under that section or misbranded under section 502 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 exclusivity under clause (iii) or (iv) of section 505(j)(5)(F).

(2) LABELING.—Notwithstanding clauses (iii) and (iv) of section 505(j)(5)(F), the Secretary may require that the labeling of a drug approved under section 505(j) that omits a pediatric indication or other aspect of labeling as described in paragraph (1) include—

(A) a statement that, because of marketing exclusivity for a manufacturer—

(i) the drug is not labeled for pediatric use; or

(ii) in the case of a drug for which there is an additional pediatric use not referred to in paragraph (1), the drug is not labeled for the pediatric use under paragraph (1); and

(B) a statement of any appropriate pediatric contraindications, warnings, precautions, or other information that the Secretary considers necessary to assure safe use.

(3) PRESERVATION OF PEDIATRIC EXCLUSIVITY AND OTHER PROVISIONS.—This subsection does not affect—

(A) the availability or scope of exclusivity under this section;

(B) the availability or scope of exclusivity under section 505 for pediatric formulations;

(C) the question of the eligibility for approval of any application under section 505(j) that omits any other conditions of approval entitled to exclusivity under clause (iii) or (iv) of section 505(j)(5)(F); or

(D) except as expressly provided in paragraphs (1) and (2), the operation of section 505.

(p) INSTITUTE OF MEDICINE STUDY.—Not later than 3 years after the date of enactment of the Best Pharmaceuticals for Children Act of 2007, the Secretary shall enter into a contract with the Institute of Medicine to conduct a study and report to Congress regarding the written requests made and the studies conducted pursuant to this section. The Institute of Medicine may devise an appropriate mechanism to review a representative sample of requests made and studies conducted pursuant to this section in order to conduct such study. Such study shall—

(1) review such representative written requests issued by the Secretary since 1997 under subsections (b) and (c);

(2) review and assess such representative pediatric studies conducted under subsections (b) and (c) since 1997 and labeling changes made as a result of such studies;

(3) review the use of extrapolation for pediatric subpopulations, the use of alternative endpoints for pediatric populations, neonatal assessment tools, and ethical issues in pediatric clinical trials;

(4) review and assess the number and importance of biological products for children that are being tested as a result of the amendments made by the Biologics Price Competition and Innovation Act of 2009 and the importance for children, health care providers, parents, and others of labeling changes made as a result of such testing;

(5) review and assess the number, importance, and prioritization of any biological products that are not being tested for pediatric use; and

(6) offer recommendations for ensuring pediatric testing of biological products, including consideration of any incentives, such as those provided under this section or section 351(m) of the Public Health Service Act.

SEC. 409I. [284m] PROGRAM FOR PEDIATRIC STUDIES OF DRUGS.

(a) LIST OF PRIORITY ISSUES IN PEDIATRIC THERAPEUTICS.—

(1) **IN GENERAL.**—Not later than one year after the date of enactment of the Best Pharmaceuticals for Children Act of 2007, the Secretary, acting through the Director of the National Institutes of Health and in consultation with the Commissioner of Food and Drugs and experts in pediatric research, shall develop and publish a priority list of needs in pediatric therapeutics, including drugs, biological products, or indications that require study. The list shall be revised every three years.

(2) **CONSIDERATION OF AVAILABLE INFORMATION.**—In developing and prioritizing the list under paragraph (1), the Secretary shall consider—

(A) therapeutic gaps in pediatrics that may include developmental pharmacology, pharmacogenetic determinants of drug response, metabolism of drugs and biologics in children, and pediatric clinical trials;

(B) particular pediatric diseases, disorders or conditions where more complete knowledge and testing of therapeutics, including drugs and biologics, may be beneficial in pediatric populations; and

(C) the adequacy of necessary infrastructure to conduct pediatric pharmacological research, including research networks and trained pediatric investigators.

(b) **PEDIATRIC STUDIES AND RESEARCH.**—The Secretary, acting through the National Institutes of Health, shall award funds to entities that have the expertise to conduct pediatric clinical trials or other research (including qualified universities, hospitals, laboratories, contract research organizations, practice groups, federally funded programs such as pediatric pharmacology research units, other public or private institutions, or individuals) to enable the entities to conduct the drug studies or other research on the issues described in subsection (a). The Secretary may use contracts, grants, or other appropriate funding mechanisms to award funds under this subsection.

(c) PROCESS FOR PROPOSED PEDIATRIC STUDY REQUESTS AND LABELING CHANGES.—

(1) **SUBMISSION OF PROPOSED PEDIATRIC STUDY REQUEST.**—The Director of the National Institutes of Health shall, as appropriate, submit proposed pediatric study requests for consideration by the Commissioner of Food and Drugs for pediatric studies of a specific pediatric indication identified under subsection (a). Such a proposed pediatric study request shall be made in a manner equivalent to a written request made under subsection (b) or (c) of section 505A of the Federal Food, Drug, and Cosmetic Act or section 351(m) of this Act, including with respect to the information provided on the pediatric studies to be conducted pursuant to the request. The Director of the National Institutes of Health may submit a proposed pediatric study request for a drug for which—

(A)

(i) there is an approved application under section 505(j) of the Federal Food, Drug, and Cosmetic Act or section 351(m) of this Act; or

(ii) there is a submitted application that could be approved under the criteria of such section; and

(B) there remains no patent listed pursuant to section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act, and every three-year and five-year period referred to in subsection (c)(3)(E)(ii), (c)(3)(E)(iii), (c)(3)(E)(iv), (j)(5)(F)(ii), (j)(5)(F)(iii), or (j)(5)(F)(iv) of section 505 of the Federal Food, Drug, and Cosmetic Act, or applicable twelve-year period referred to in section 351(k)(7) of this Act, and any seven-year period referred to in section 527 of the Federal Food, Drug, and Cosmetic Act has ended for at least one form of the drug; and

(C) additional studies are needed to assess the safety and effectiveness of the use of the drug in the pediatric population.

(2) **WRITTEN REQUEST TO HOLDERS OF APPROVED APPLICATIONS.**—The Commissioner of Food and Drugs, in consultation with the Director of the National Institutes of Health, may issue a written request based on the proposed pediatric study request for the indication or indications submitted pursuant to paragraph (1) (which shall include a timeframe for negotiations for an agreement) for pediatric studies concerning a drug identified under subsection (a) to all holders of an approved application for the drug. Such a written request shall be made in a manner equivalent to the manner in which a written request is made under subsection (b) or (c) of section 505A of the Federal Food, Drug, and Cosmetic Act or section 351(m) of this Act, including with respect to information provided on the pediatric studies to be conducted pursuant to the request and using appropriate formulations for each age group for which the study is requested.

(3) **REQUESTS FOR PROPOSALS.**—If the Commissioner of Food and Drugs does not receive a response to a written request issued under paragraph (2) not later than 30 days after the date on which a request was issued, the Secretary, acting through the Director of the National Institutes of Health and in consultation with the Commissioner of Food and Drugs, shall publish a request for proposals to conduct the

pediatric studies described in the written request in accordance with subsection (b).

(4) DISQUALIFICATION.—A holder that receives a first right of refusal shall not be entitled to respond to a request for proposals under paragraph (3).

(5) CONTRACTS, GRANTS, OR OTHER FUNDING MECHANISMS.—A contract, grant, or other funding may be awarded under this section only if a proposal 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.

(6) REPORTING OF STUDIES.—

(A) IN GENERAL.—On completion of a pediatric study in accordance with an award under this section, a report concerning the study shall be submitted to the Director of the National Institutes of Health and the Commissioner of Food and Drugs. The report shall include all data generated in connection with the study, including a written request if issued.

(B) AVAILABILITY OF REPORTS.—Each report submitted under subparagraph (A) shall be considered to be in the public domain (subject to section 505A(d)(4) of the Federal Food, Drug, and Cosmetic Act) and shall be assigned a docket number by the Commissioner of Food and Drugs. An interested person may submit written comments concerning such pediatric studies to the Commissioner of Food and Drugs, and the written comments shall become part of the docket file with respect to each of the drugs.

(C) ACTION BY COMMISSIONER.—The Commissioner of Food and Drugs shall take appropriate action in response to the reports submitted under subparagraph (A) in accordance with paragraph (7).

(7) REQUESTS FOR LABELING CHANGE.—During the 180-day period after the date on which a report is submitted under paragraph (6)(A), the Commissioner of Food and Drugs shall—

(A) review the report and such other data as are available concerning the safe and effective use in the pediatric population of the drug studied;

(B) negotiate with the holders of approved applications for the drug studied for any labeling changes that the Commissioner of Food and Drugs determines to be appropriate and requests the holders to make; and

(C)

(i) place in the public docket file a copy of the report and of any requested labeling changes; and

(ii) publish in the Federal Register and through a posting on the Web site of the Food and Drug Administration a summary of the report and a copy of any requested labeling changes.

(8) DISPUTE RESOLUTION.—

(A) REFERRAL TO PEDIATRIC ADVISORY COMMITTEE.—If, not later than the end of the 180-day period specified in paragraph (7), the holder of an approved application for the drug involved does not agree to any labeling change requested by the Commissioner of Food and Drugs under that paragraph, the Commissioner of Food and Drugs shall refer the request to the Pediatric Advisory Committee.

(B) ACTION BY THE PEDIATRIC ADVISORY COMMITTEE.—Not later than 90 days after receiving a referral under subparagraph (A), the Pediatric Advisory Committee shall—

(i) 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

(ii) make a recommendation to the Commissioner of Food and Drugs as to appropriate labeling changes, if any.

(9) FDA DETERMINATION.—Not later than 30 days after receiving a recommendation from the Pediatric Advisory Committee under paragraph (8)(B)(ii) with respect to a drug, the Commissioner of Food and Drugs 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 of Food and Drugs determines to be appropriate.

(10) FAILURE TO AGREE.—If a holder of an approved application for a drug, within 30 days after receiving a request to make a labeling change under paragraph (9), does not agree to make a requested labeling change, the Commissioner of Food and Drugs may deem the drug to be misbranded under the Federal Food, Drug, and Cosmetic Act.

(11) NO EFFECT ON AUTHORITY.—Nothing in this subsection limits the authority of the United States to bring an enforcement action under the Federal Food, Drug, and Cosmetic Act 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.

(d) **DISSEMINATION OF PEDIATRIC INFORMATION.**—Not later than one year after the date of enactment of the Best Pharmaceuticals for Children Act of 2007, the Secretary, acting through the Director of the National Institutes of Health, shall study the feasibility of establishing a compilation of information on pediatric drug use and report the findings to Congress.

(e) **AUTHORIZATION OF APPROPRIATIONS.**—

(1) **IN GENERAL.**—There are authorized to be appropriated to carry out this section, \$25,000,000 for each of fiscal years 2013 through 2017.

Best Pharmaceuticals for Children Act: Biologics
Sec. 351(m) of the Public Health Service Act [42 U.S.C. 262(m)]

(m) **PEDIATRIC STUDIES.**—

(1) **APPLICATION OF CERTAIN PROVISIONS.**—The provisions of subsections (a), (d), (e), (f), (h), (i), (j), (k), (l), (n), and (p) of section 505A of the Federal Food, Drug, and Cosmetic Act shall apply with respect to the extension of a period under paragraphs (2) and (3) to the same extent and in the same manner as such provisions apply with respect to the extension of a period under subsection (b) or (c) of section 505A of the Federal Food, Drug, and Cosmetic Act.

(2) **MARKET EXCLUSIVITY FOR NEW BIOLOGICAL PRODUCTS.**—If, prior to approval of an application that is submitted under subsection (a), the Secretary determines that information relating to the use of a new biological product 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), the applicant agrees to the request, such studies are completed using appropriate formulations for each age group for which the study is requested within any such timeframe, and the reports thereof are submitted and accepted in accordance with section 505A(d)(3) of the Federal Food, Drug, and Cosmetic Act—

(A) the periods for such biological product referred to in subsection (k)(7) are deemed to be 4 years and 6 months rather than 4 years and 12 years and 6 months rather than 12 years; and

(B) if the biological product is designated under section 526 for a rare disease or condition, the period for such biological product referred to in section 527(a) is deemed to be 7 years and 6 months rather than 7 years.

(3) **MARKET EXCLUSIVITY FOR ALREADY-MARKETED BIOLOGICAL PRODUCTS.**—If the Secretary determines that information relating to the use of a licensed biological product in the pediatric population may produce health benefits in that population and makes a written request to the holder of an approved application under subsection (a) for pediatric studies (which shall include a timeframe for completing such studies), the holder agrees to the request, such studies are completed using appropriate formulations for each age group for which the study is requested within any such timeframe, and the reports thereof are submitted and accepted in accordance with section 505A(d)(3) of the Federal Food, Drug, and Cosmetic Act—

(A) the periods for such biological product referred to in subsection (k)(7) are deemed to be 4 years and 6 months rather than 4 years and 12 years and 6 months rather than 12 years; and

(B) if the biological product is designated under section 526 for a rare disease or condition, the period for such biological product referred to in section 527(a) is deemed to be 7 years and 6 months rather than 7 years.

(4) **EXCEPTION.**—The Secretary shall not extend a period referred to in paragraph (2)(A), (2)(B), (3)(A), or (3)(B) if the determination under section 505A(d)(3) is made later than 9 months prior to the expiration of such period.

Pediatric Research Equity Act
Sec. 505B of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355c]

SEC. 505B. [355c] RESEARCH INTO PEDIATRIC USES FOR DRUGS AND BIOLOGICAL PRODUCTS.

(a) **NEW DRUGS AND BIOLOGICAL PRODUCTS.**—

(1) **IN GENERAL.**—A person that submits, on or after the date of enactment of the Pediatric Research Equity Act of 2007, an application (or supplement to an application) for a drug—

(A) under section 505 for a new active ingredient, new indication, new dosage form, new dosing regimen, or new route of administration,

or

(B) under section 351 of the Public Health Service Act (42 U.S.C. 262) for a new active ingredient, new indication, new dosage form, new dosing regimen, or new route of administration,

shall submit with the application the assessments described in paragraph (2).

(2) ASSESSMENTS.—

(A) IN GENERAL.—The assessments referred to in paragraph (1) shall contain data, gathered using appropriate formulations for each age group for which the assessment is required, that are adequate—

- (i) to assess the safety and effectiveness of the drug or the biological product for the claimed indications in all relevant pediatric subpopulations; and
- (ii) to support dosing and administration for each pediatric subpopulation for which the drug or the biological product is safe and effective.

(B) SIMILAR COURSE OF DISEASE OR SIMILAR EFFECT OF DRUG OR BIOLOGICAL PRODUCT.—

(i) IN GENERAL.—If the course of the disease and the effects of the drug are sufficiently similar in adults and pediatric patients, the Secretary may conclude that pediatric effectiveness can be extrapolated from adequate and well-controlled studies in adults, usually supplemented with other information obtained in pediatric patients, such as pharmacokinetic studies.

(ii) EXTRAPOLATION BETWEEN AGE GROUPS.—A study may not be needed in each pediatric age group if data from one age group can be extrapolated to another age group.

(iii) INFORMATION ON EXTRAPOLATION.—A brief documentation of the scientific data supporting the conclusion under clauses (i) and (ii) shall be included in any pertinent reviews for the application under section 505 or section 351 of the Public Health Service Act (42 U.S.C. 262).

(3) DEFERRAL

(A) IN GENERAL.—On the initiative of the Secretary or at the request of the applicant, the Secretary may defer submission of some or all assessments required under paragraph (1) until a specified date after approval of the drug or issuance of the license for a biological product if—

(i) the Secretary finds that—

- (I) the drug or biological product is ready for approval for use in adults before pediatric studies are complete;
- (II) pediatric studies should be delayed until additional safety or effectiveness data have been collected; or
- (III) there is another appropriate reason for deferral; and

(ii) the applicant submits to the Secretary—

- (I) certification of the grounds for deferring the assessments;
- (II) a pediatric study plan as described in subsection (e);
- (III) evidence that the studies are being conducted or will be conducted with due diligence and at the earliest possible time; and
- (IV) a timeline for the completion of such studies.

(B) DEFERRAL EXTENSION.—

(i) IN GENERAL.—On the initiative of the Secretary or at the request of the applicant, the Secretary may grant an extension of a deferral approved under subparagraph (A) for submission of some or all assessments required under paragraph (1) if—

- (I) the Secretary determines that the conditions described in subclause (II) or (III) of subparagraph (A)(i) continue to be met; and
- (II) the applicant submits a new timeline under subparagraph (A)(ii)(IV) and any significant updates to the information required under subparagraph (A)(ii).

(ii) TIMING AND INFORMATION.—If the deferral extension under this subparagraph is requested by the applicant, the applicant shall submit the deferral extension request containing the information described in this subparagraph not less than 90 days prior to the date that the deferral would expire. The Secretary shall respond to such request not later than 45 days after the receipt of such letter. If the Secretary grants such an extension, the specified date shall be the extended date. The sponsor of the required assessment under paragraph (1) shall not be issued a letter described in subsection (d) unless the specified or extended date of submission for such required studies has passed or if the request for an extension is pending. For a deferral that has expired prior to the date of enactment of the Food and Drug Administration Safety and Innovation Act or that will expire prior to 270 days after the date of enactment of such Act, a deferral extension shall be requested by an applicant not later than 180 days after the date of enactment of such Act. The Secretary shall respond to any such request as soon as practicable, but not later than 1 year after the date of enactment of such Act. Nothing in this clause shall prevent the Secretary from updating the status of a study or studies publicly if components of such study or studies are late or delayed.

(C) ANNUAL REVIEW.—

(i) IN GENERAL.—On an annual basis following the approval of a deferral under subparagraph (A), the applicant shall submit to the Secretary the following information:

(I) Information detailing the progress made in conducting pediatric studies.

(II) If no progress has been made in conducting such studies, evidence and documentation that such studies will be conducted with due diligence and at the earliest possible time.

(III) Projected completion date for pediatric studies.

(IV) The reason or reasons why a deferral or deferral extension continues to be necessary.

(ii) PUBLIC AVAILABILITY.—Not later than 90 days after the submission to the Secretary of the information submitted through the annual review under clause (i), the Secretary shall make available to the public in an easily accessible manner, including through the Internet Web site of the Food and Drug Administration—

(I) such information;

(II) the name of the applicant for the product subject to the assessment;

(III) the date on which the product was approved; and

(IV) the date of each deferral or deferral extension under this paragraph for the product.

(4) WAIVERS.—

(A) FULL WAIVER.—On the initiative of the Secretary or at the request of an applicant, the Secretary shall grant a full waiver, as appropriate, of the requirement to submit assessments for a drug or biological product under this subsection if the applicant certifies and the Secretary finds that—

(i) necessary studies are impossible or highly impracticable (because, for example, the number of patients is so small or the patients are geographically dispersed);

(ii) there is evidence strongly suggesting that the drug or biological product would be ineffective or unsafe in all pediatric age groups;
or

(iii) the drug or biological product—

(I) does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients; and

(II) is not likely to be used in a substantial number of pediatric patients.

(B) PARTIAL WAIVER.—On the initiative of the Secretary or at the request of an applicant, the Secretary shall grant a partial waiver, as appropriate, of the requirement to submit assessments for a drug or biological product under this subsection with respect to a specific pediatric age group if the applicant certifies and the Secretary finds that—

(i) 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);

(ii) there is evidence strongly suggesting that the drug or biological product would be ineffective or unsafe in that age group;

(iii) the drug or biological product—

(I) does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients in that age group; and

(II) is not likely to be used by a substantial number of pediatric patients in that age group; or

(iv) the applicant can demonstrate that reasonable attempts to produce a pediatric formulation necessary for that age group have failed.

(C) PEDIATRIC FORMULATION NOT POSSIBLE.—If a partial waiver is granted on the ground that it is not possible to develop a pediatric formulation, the waiver shall cover only the pediatric groups requiring that formulation. An applicant seeking such a partial waiver shall submit to the Secretary documentation detailing why a pediatric formulation cannot be developed and, if the waiver is granted, the applicant's submission shall promptly be made available to the public in an easily accessible manner, including through posting on the Web site of the Food and Drug Administration.

(D) LABELING REQUIREMENT.—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.

(b) MARKETED DRUGS AND BIOLOGICAL PRODUCTS.—

(1) IN GENERAL.—The Secretary may (by order in the form of a letter) require the sponsor or holder of an approved application for a drug under section 505 or the holder of a license for a biological product under section 351 of the Public Health Service Act (42 U.S.C. 262) to submit by a specified date the assessments described in subsection (a)(2), if the Secretary finds that—

(A)

(i) the drug or biological product is used for a substantial number of pediatric patients for the labeled indications; and

(ii) adequate pediatric labeling could confer a benefit on pediatric patients;

(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 1 or more of the claimed indications; or

(C) the absence of adequate pediatric labeling could pose a risk to pediatric patients.

(2) WAIVERS.—

(A) FULL WAIVER.—At the request of an applicant, 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—

(i) 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

(ii) there is evidence strongly suggesting that the drug or biological product would be ineffective or unsafe in all pediatric age groups.

(B) PARTIAL WAIVER.—At the request of an applicant, 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—

(i) 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);

(ii) there is evidence strongly suggesting that the drug or biological product would be ineffective or unsafe in that age group;

(iii)

(I) the drug or biological product—

(aa) does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients in that age group; and

(bb) is not likely to be used in a substantial number of pediatric patients in that age group; and

(II) the absence of adequate labeling could not pose significant risks to pediatric patients; or

(iv) the applicant can demonstrate that reasonable attempts to produce a pediatric formulation necessary for that age group have failed.

(C) PEDIATRIC FORMULATION NOT POSSIBLE.—If a waiver is granted on the ground that it is not possible to develop a pediatric formulation, the waiver shall cover only the pediatric groups requiring that formulation. An applicant seeking either a full or partial waiver shall submit to the Secretary documentation detailing why a pediatric formulation cannot be developed and, if the waiver is granted, the applicant's submission shall promptly be made available to the public in an easily accessible manner, including through posting on the Web site of the Food and Drug Administration.

(D) LABELING REQUIREMENT.—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.

(3) EFFECT OF SUBSECTION.— Nothing in this subsection alters or amends section 301(j) of this Act or section 552 of title 5 or section 1905 of title 18, United States Code.

(c) MEANINGFUL THERAPEUTIC BENEFIT.—For the purposes of paragraph (4)(A)(iii)(I) and (4)(B)(iii)(I) of subsection (a) and paragraphs (1)(B) and (2)(B)(iii)(I)(aa) of subsection (b), a drug or biological product shall be considered to represent a meaningful therapeutic benefit over existing therapies if the Secretary determines that—

(1) if approved, the drug or biological product could represent an 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.

(d) SUBMISSION OF ASSESSMENTS.—If a person fails to submit a required assessment described in subsection (a)(2), fails to meet the applicable requirements in subsection (a)(3), or fails to submit a request for approval of a pediatric formulation described in subsection (a) or (b), in accordance with applicable provisions of subsections (a) and (b), the following shall apply:

(1) Beginning 270 days after the date of enactment of the Food and Drug Administration Safety and Innovation Act, the Secretary shall issue a non-compliance letter to such person informing them of such failure to submit or meet the requirements of the applicable subsection. Such letter shall require the person to respond in writing within 45 calendar days of issuance of such letter. Such response may include the person's request for a deferral extension if applicable. Such letter and the person's written response to such letter shall be made publicly available on the Internet Web site of the Food and Drug Administration 60 calendar days after issuance, with redactions for any trade secrets and confidential commercial information. If the Secretary determines that the letter was issued in error, the requirements of this paragraph shall not apply.

(2) The drug or biological product that is the subject of an assessment described in subsection (a)(2), applicable requirements in subsection (a)(3), or request for approval of a pediatric formulation, may be considered misbranded solely because of that failure and subject to relevant enforcement action (except that the drug or biological product shall not be subject to action under section 303), but such failure shall not be the basis for a proceeding—

(A) to withdraw approval for a drug under section 505(e); or

(B) to revoke the license for a biological product under section 351 of the Public Health Service Act.

(e) PEDIATRIC STUDY PLANS.—

(1) IN GENERAL.—An applicant subject to subsection (a) shall submit to the Secretary an initial pediatric study plan prior to the submission of the assessments described under subsection (a)(2).

(2) TIMING; CONTENT; MEETING.—

(A) TIMING.—An applicant shall submit the initial pediatric plan under paragraph (1)—

(i) before the date on which the applicant submits the assessments under subsection (a)(2); and

(ii) not later than—

(I) 60 calendar days after the date of the end-of-Phase 2 meeting (as such term is used in section 312.47 of title 21, Code of Federal Regulations, or successor regulations); or

(II) such other time as may be agreed upon between the Secretary and the applicant.

Nothing in this section shall preclude the Secretary from accepting the submission of an initial pediatric plan earlier than the date

otherwise applicable under this subparagraph.

(B) CONTENT OF INITIAL PLAN.—The initial pediatric study plan shall include—

- (i) an outline of the pediatric study or studies that the applicant plans to conduct (including, to the extent practicable study objectives and design, age groups, relevant endpoints, and statistical approach);
- (ii) any request for a deferral, partial waiver, or waiver under this section, if applicable, along with any supporting information; and
- (iii) other information specified in the regulations promulgated under paragraph (7).

(C) MEETING.—The Secretary—

- (i) shall meet with the applicant to discuss the initial pediatric study plan as soon as practicable, but not later than 90 calendar days after the receipt of such plan under subparagraph (A);
- (ii) may determine that a written response to the initial pediatric study plan is sufficient to communicate comments on the initial pediatric study plan, and that no meeting is necessary; and
- (iii) if the Secretary determines that no meeting is necessary, shall so notify the applicant and provide written comments of the Secretary as soon as practicable, but not later than 90 calendar days after the receipt of the initial pediatric study plan.

(3) AGREED INITIAL PEDIATRIC STUDY PLAN.—Not later than 90 calendar days following the meeting under paragraph (2)(C)(i) or the receipt of a written response from the Secretary under paragraph (2)(C)(iii), the applicant shall document agreement on the initial pediatric study plan in a submission to the Secretary marked 'Agreed Initial Pediatric Study Plan', and the Secretary shall confirm such agreement to the applicant in writing not later than 30 calendar days of receipt of such agreed initial pediatric study plan.

(4) DEFERRAL AND WAIVER.—If the agreed initial pediatric study plan contains a request from the applicant for a deferral, partial waiver, or waiver under this section, the written confirmation under paragraph (3) shall include a recommendation from the Secretary as to whether such request meets the standards under paragraphs (3) or (4) of subsection (a).

(5) AMENDMENTS TO THE PLAN.—At the initiative of the Secretary or the applicant, the agreed initial pediatric study plan may be amended at any time. The requirements of paragraph (2)(C) shall apply to any such proposed amendment in the same manner and to the same extent as such requirements apply to an initial pediatric study plan under paragraph (1). The requirements of paragraphs (3) and (4) shall apply to any agreement resulting from such proposed amendment in the same manner and to the same extent as such requirements apply to an agreed initial pediatric study plan.

(6) INTERNAL COMMITTEE.—The Secretary shall consult the internal committee under section 505C on the review of the initial pediatric study plan, agreed initial pediatric plan, and any significant amendments to such plans.

(7) REQUIRED RULEMAKING.—Not later than 1 year after the date of enactment of the Food and Drug Administration Safety and Innovation Act, the Secretary shall promulgate proposed regulations and issue guidance to implement the provisions of this subsection.

(f) REVIEW OF PEDIATRIC STUDY PLANS, ASSESSMENTS, DEFERRALS, DEFERRAL EXTENSIONS, AND WAIVERS.—

(1) REVIEW.—Beginning not later than 30 days after the date of enactment of the Pediatric Research Equity Act of 2007, the Secretary shall utilize the internal committee established under section 505C to provide consultation to reviewing divisions on initial pediatric study plans, agreed initial pediatric study plans, and assessments prior to approval of an application or supplement for which a pediatric assessment is required under this section and all deferral, deferral extension and waiver requests granted pursuant to this section.

(2) ACTIVITY BY COMMITTEE.—The committee referred to in paragraph (1) may operate using appropriate members of such committee and need not convene all members of the committee.

(3) DOCUMENTATION OF COMMITTEE ACTION.—For each drug or biological product, the committee referred to in paragraph (1) shall document, for each activity described in paragraph (4) or (5), which members of the committee participated in such activity.

(4) REVIEW OF PEDIATRIC STUDY PLANS, ASSESSMENTS, DEFERRALS, DEFERRAL EXTENSIONS AND WAIVERS.—Consultation on initial pediatric study plans, agreed initial pediatric study plans, and assessments by the committee referred to in paragraph (1) pursuant to this section shall occur prior to approval of an application or supplement for which a pediatric assessment is required under this section. The committee shall review all requests for deferrals, deferral extensions, and waivers from the requirement to submit a pediatric assessment granted under this section and shall provide recommendations as needed to reviewing divisions, including with respect to whether such a supplement, when submitted, shall be considered for priority review.

(5) RETROSPECTIVE REVIEW OF PEDIATRIC ASSESSMENTS, DEFERRALS, AND WAIVERS.—Not later than 1 year after the date of enactment of the Pediatric Research Equity Act of 2007, the committee referred to in paragraph (1) shall conduct a retrospective review

and analysis of a representative sample of assessments submitted and deferrals and waivers approved under this section since December 3, 2003. Such review shall include an analysis of the quality and consistency of pediatric information in pediatric assessments and the appropriateness of waivers and deferrals granted. Based on such review, the Secretary shall issue recommendations to the review divisions for improvements and initiate guidance to industry related to the scope of pediatric studies required under this section.

(6) TRACKING OF ASSESSMENTS AND LABELING CHANGES.—The Secretary, in consultation with the committee referred to in paragraph (1), shall track and make available to the public in an easily accessible manner, including through posting on the Web site of the Food and Drug Administration—

(A) the number of assessments conducted under this section;

(B) the specific drugs and biological products and their uses assessed under this section;

(C) the types of assessments conducted under this section, including trial design, the number of pediatric patients studied, and the number of centers and countries involved;

(D) aggregated on an annual basis—

(i) the total number of deferrals and deferral extensions requested and granted under this section and, if granted, the reasons for each such deferral or deferral extension;

(ii) the timeline for completion of the assessments;

(iii) the number of assessments completed and pending; and

(iv) the number of postmarket non-compliance letters issued pursuant to subsection (d), and the recipients of such letters;

(E) the number of waivers requested and granted under this section and, if granted, the reasons for the waivers;

(F) the number of pediatric formulations developed and the number of pediatric formulations not developed and the reasons any such formulation was not developed;

(G) the labeling changes made as a result of assessments conducted under this section;

(H) an annual summary of labeling changes made as a result of assessments conducted under this section for distribution pursuant to subsection (h)(2);

(I) an annual summary of information submitted pursuant to subsection (a)(3)(B); and

(J) the number of times the committee referred to in paragraph (1) made a recommendation to the Secretary under paragraph (4) regarding priority review, the number of times the Secretary followed or did not follow such a recommendation, and, if not followed, the reasons why such a recommendation was not followed.

(g) LABELING CHANGES.—

(1) DISPUTE RESOLUTION.—

(A) REQUEST FOR LABELING CHANGE AND FAILURE TO AGREE.—If, on or after the date of enactment of the Pediatric Research Equity Act of 2007, the Commissioner determines that a sponsor and the Commissioner have been unable to reach agreement on appropriate changes to the labeling for the drug that is the subject of the application or supplement, not later than 180 days after the date of the submission of the application or supplement that receives a priority review or 330 days after the date of the submission of an application or supplement that receives a standard review—

(i) the Commissioner shall request that the sponsor of the application make any labeling change that the Commissioner determines to be appropriate; and

(ii) if the sponsor does not agree within 30 days after the Commissioner's request to make a labeling change requested by the Commissioner, the Commissioner shall refer the matter to the Pediatric Advisory Committee.

(B) ACTION BY THE PEDIATRIC ADVISORY COMMITTEE.—Not later than 90 days after receiving a referral under subparagraph (A)(ii), the Pediatric Advisory Committee shall—

(i) review the pediatric study reports; and

(ii) make a recommendation to the Commissioner concerning appropriate labeling changes, if any.

(C) CONSIDERATION OF RECOMMENDATIONS.—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 or supplement to make any labeling changes that the Commissioner determines to be appropriate.

(D) MISBRANDING.—If the sponsor of the application or supplement, within 30 days after receiving a request under subparagraph (C), 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 or supplement to be misbranded.

(E) NO EFFECT ON AUTHORITY.—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.

(2) OTHER LABELING CHANGES.—If, on or after the date of enactment of the Pediatric Research Equity Act of 2007, the Secretary makes a determination that a pediatric assessment conducted under this section does or does not demonstrate that the drug that is the subject of such assessment is safe and effective in pediatric populations or subpopulations, including whether such assessment results are inconclusive, the Secretary shall order the labeling of such product to include information about the results of the assessment and a statement of the Secretary's determination.

(h) DISSEMINATION OF PEDIATRIC INFORMATION.—

(1) IN GENERAL.—Not later than 210 days after the date of submission of an application (or supplement to an application) that contains a pediatric assessment under this section, if the application (or supplement) receives a priority review, or not later than 330 days after the date of submission of an application (or supplement to an application) that contains a pediatric assessment under this section, if the application (or supplement) receives a standard review, the Secretary shall make available to the public in an easily accessible manner the medical, statistical, and clinical pharmacology reviews of such pediatric assessments, and shall post such assessments on the Web site of the Food and Drug Administration.

(2) DISSEMINATION OF INFORMATION REGARDING LABELING CHANGES.—Beginning on the date of enactment of the Pediatric Research Equity Act of 2007, the Secretary shall require that the sponsors of the assessments that result in labeling changes that are reflected in the annual summary developed pursuant to subsection (f)(6)(H) distribute such information to physicians and other health care providers.

(3) EFFECT OF SUBSECTION.— Nothing in this subsection alters or amends section 301(j) of this Act or section 552 of title 5 or section 1905 of title 18, United States Code.

(i) ADVERSE EVENT REPORTING.—

(1) REPORTING IN FIRST 18-MONTH PERIOD.—Beginning on the date of enactment of the Pediatric Research Equity Act of 2007, during the 18-month period beginning on the date a labeling change is made pursuant to subsection (g), the Secretary shall ensure that all adverse event reports that have been received for such drug (regardless of when such report was received) are referred to the Office of Pediatric Therapeutics. In considering such reports, the Director of such Office shall provide for the review of such reports by the Pediatric Advisory Committee, including obtaining any recommendations of such committee regarding whether the Secretary should take action under this chapter in response to such reports.

(2) REPORTING IN SUBSEQUENT PERIODS.—Following the 18-month period described in paragraph (1), the Secretary shall, as appropriate, refer to the Office of Pediatric Therapeutics all pediatric adverse event reports for a drug for which a pediatric study was conducted under this section. In considering such reports, the Director of such Office may provide for the review of such reports by the Pediatric Advisory Committee, including obtaining any recommendation of such Committee regarding whether the Secretary should take action in response to such reports.

(3) PRESERVATION OF AUTHORITY.—Nothing in this subsection shall prohibit the Office of Pediatric Therapeutics from providing for the review of adverse event reports by the Pediatric Advisory Committee prior to the 18-month period referred to in paragraph (1), if such review is necessary to ensure safe use of a drug in a pediatric population.

(4) EFFECT.—The requirements of this subsection shall supplement, not supplant, other review of such adverse event reports by the Secretary.

(j) SCOPE OF AUTHORITY.—Nothing in this section provides to the Secretary any authority to require a pediatric assessment of any drug or biological product, or any assessment regarding other populations or uses of a drug or biological product, other than the pediatric assessments described in this section.

(k) 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 section 526.

(l) INSTITUTE OF MEDICINE STUDY.—

(1) IN GENERAL.—Not later than three years after the date of enactment of the Pediatric Research Equity Act of 2007, the Secretary shall contract with the Institute of Medicine to conduct a study and report to Congress regarding the pediatric studies conducted pursuant to this section or precursor regulations since 1997 and labeling changes made as a result of such studies.

(2) CONTENT OF STUDY.—The study under paragraph (1) shall review and assess the use of extrapolation for pediatric subpopulations, the use of alternative endpoints for pediatric populations, neonatal assessment tools, the number and type of pediatric adverse events, and ethical issues in pediatric clinical trials.

(3) REPRESENTATIVE SAMPLE.—The Institute of Medicine may devise an appropriate mechanism to review a representative sample of studies conducted pursuant to this section from each review division within the Center for Drug Evaluation and Research in order to make the requested assessment.

(m) NEW ACTIVE INGREDIENT.—

(1) NON-INTERCHANGEABLE BIOSIMILAR BIOLOGICAL PRODUCT.—A biological product that is biosimilar to a reference product under section 351 of the Public Health Service Act, and that the Secretary has not determined to meet the standards described in subsection (k)(4) of such section for interchangeability with the reference product, shall be considered to have a new active ingredient under this section.

(2) INTERCHANGEABLE BIOSIMILAR BIOLOGICAL PRODUCT.—A biological product that is interchangeable with a reference product under section section 351 of the Public Health Service Act shall not be considered to have a new active ingredient under this section.

Pediatric Review Committee

Sec. 505C of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355d)

SEC. 505C. [355d] INTERNAL COMMITTEE FOR REVIEW OF PEDIATRIC PLANS, ASSESSMENTS, DEFERRALS, DEFERRAL EXTENSIONS, AND WAIVERS.

The Secretary shall establish an internal committee within the Food and Drug Administration to carry out the activities as described in sections 505A(f) and 505B(f). Such internal committee shall include employees of the Food and Drug Administration, with expertise in pediatrics (including representation from the Office of Pediatric Therapeutics), biopharmacology, statistics, chemistry, legal issues, pediatric ethics, neonatology, and the appropriate expertise pertaining to the pediatric product under review, such as expertise in child and adolescent psychiatry, and other individuals designated by the Secretary.

Office of Pediatric Therapeutics

Sec. 6(c) of the Best Pharmaceuticals for Children Act [21 U.S.C. 393a]

SEC. 1003a. [393a] OFFICE OF PEDIATRIC THERAPEUTICS.

(a) ESTABLISHMENT.—The Secretary of Health and Human Services shall establish an Office of Pediatric Therapeutics within the Food and Drug Administration.

(b) DUTIES.—The Office of Pediatric Therapeutics shall be responsible for coordination and facilitation of all activities of the Food and Drug Administration that may have any effect on a pediatric population or the practice of pediatrics or may in any other way involve pediatric issues, including increasing pediatric access to medical devices.

(c) STAFF.—The staff of the Office of Pediatric Therapeutics shall coordinate with employees of the Department of Health and Human Services who exercise responsibilities relating to pediatric therapeutics and shall include—

(1) one or more additional individuals with expertise concerning ethical issues presented by the conduct of clinical research in the pediatric population;

(2) subject to subsection (d), one or more additional individuals with necessary expertise in a pediatric subpopulation that is, as determined through consideration of the reports and recommendations issued by the Institute of Medicine and the Comptroller General of the United States, less likely to be studied as a part of a written request issued under section 505A of the Federal Food, Drug, and Cosmetic Act or an assessment under section 505B of such Act;

(3) one or more additional individuals with expertise in pediatric epidemiology; and

(4) one or more additional individuals with expertise in pediatrics as may be necessary to perform the activities described in subsection

(b) of this section.

(d) NEONATOLOGY EXPERTISE.—For the 5-year period beginning on the date of enactment of this subsection, at least one of the individuals described in subsection (c)(2) shall have expertise in neonatology.

Other BPCA/PREA Provisions

Food and Drug Administration Safety and Innovation Act (PL 112-144)

SEC. 503. COMMUNICATION WITH PEDIATRIC REVIEW COMMITTEE.

Not later than 1 year after the date of enactment of this Act, the Secretary of Health and Human Services (referred to in this title as the 'Secretary') shall issue internal standard operating procedures that provide for the review by the internal review committee established under section 505C of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355d) of any significant modifications to initial pediatric study plans, agreed initial pediatric study plans, and written requests under sections 505A and 505B of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355a, 355c). Such internal standard operating procedures shall be made publicly available on the Internet Web site of the Food and Drug Administration.

SEC. 504. ACCESS TO DATA.

Not later than 3 years after the date of enactment of this Act, the Secretary shall make available to the public, including through posting on the Internet Web site of the Food and Drug Administration, the medical, statistical, and clinical pharmacology reviews of, and corresponding written requests issued to an applicant, sponsor, or holder for, pediatric studies submitted between January 4, 2002, and September 27, 2007, under subsection (b) or (c) of section 505A of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355a) for which 6 months of market exclusivity was granted and that resulted in a labeling change. The Secretary shall make public the information described in the preceding sentence in a manner consistent with how the Secretary releases information under section 505A(k) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355a(k)).

SEC. 506. PEDIATRIC STUDY PLANS

(c) EFFECTIVE DATE.—

(1) IN GENERAL.—Subject to paragraph (2), the amendments made by this section shall take effect 180 calendar days after the date of enactment of this Act, irrespective of whether the Secretary has promulgated final regulations to carry out such amendments.

(2) RULE OF CONSTRUCTION.—Paragraph (1) shall not be construed to affect the deadline for promulgation of proposed regulations under section 505B(e)(7) of the Federal Food, Drug, and Cosmetic Act, as added by subsection (a) of this section.

SEC. 508. REPORT.

(a) IN GENERAL.—Not later than four years after the date of enactment of this Act and every five years thereafter, the Secretary shall prepare and submit to the Committee on Health, Education, Labor, and Pensions of the Senate and the Committee on Energy and Commerce of the House of Representatives, and make publicly available, including through posting on the Internet Web site of the Food and Drug Administration, a report on the implementation of sections 505A and 505B of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355a, 355c).

(b) CONTENTS.—Each report under subsection (a) shall include—

(1) an assessment of the effectiveness of sections 505A and 505B of the Federal Food, Drug, and Cosmetic Act in improving information about pediatric uses for approved drugs and biological products, including the number and type of labeling changes made since the date of enactment of this Act and the importance of such uses in the improvement of the health of children;

(2) the number of required studies under such section 505B that have not met the initial deadline provided under such section 505B, including—

(A) the number of deferrals and deferral extensions granted and the reasons such extensions were granted;

(B) the number of waivers and partial waivers granted; and

(C) the number of letters issued under subsection (d) of such section 505B;

(3) an assessment of the timeliness and effectiveness of pediatric study planning since the date of enactment of this Act, including the number of initial pediatric study plans not submitted in accordance with the requirements of subsection (e) of such section 505B and any resulting rulemaking;

(4) the number of written requests issued, accepted, and declined under such section 505A since the date of enactment of this Act, and a listing of any important gaps in pediatric information as a result of such declined requests;

(5) a description and current status of referrals made under subsection (n) of such section 505A;

(6) an assessment of the effectiveness of studying biological products in pediatric populations under such sections 505A and 505B and section 409I of the Public Health Service Act (42 U.S.C. 284m);

(7)

(A) the efforts made by the Secretary to increase the number of studies conducted in the neonatal population (including efforts made to encourage the conduct of appropriate studies in neonates by companies with products that have sufficient safety and other information to make the conduct of the studies ethical and safe); and

(B) the results of such efforts;

(8)

(A) the number and importance of drugs and biological products for children with cancer that are being tested as a result of the programs under such sections 505A and 505B and under section 409I of the Public Health Service Act; and

(B) any recommendations for modifications to such programs that would lead to new and better therapies for children with cancer, including a detailed rationale for each recommendation;

(9) any recommendations for modification to such programs that would improve pediatric drug research and increase pediatric labeling of drugs and biological products;

(10) an assessment of the successes of and limitations to studying drugs for rare diseases under such sections 505A and 505B; and

(11) an assessment of the Secretary's efforts to address the suggestions and options described in any prior report issued by the Comptroller General, Institute of Medicine, or the Secretary, and any subsequent reports, including recommendations therein, regarding the topics addressed in the reports under this section, including with respect to—

(A) improving public access to information from pediatric studies conducted under such sections 505A and 505B; and

(B) improving the timeliness of pediatric studies and pediatric study planning under such sections 505A and 505B.

(c) **STAKEHOLDER COMMENT.**—At least 180 days prior to the submission of each report under subsection (a), the Secretary shall consult with representatives of patient groups (including pediatric patient groups), consumer groups, regulated industry, academia, and other interested parties to obtain any recommendations or information relevant to the report including suggestions for modifications that would improve pediatric drug research and pediatric labeling of drugs and biological products.

SEC. 509. TECHNICAL AMENDMENTS.

(g) **APPLICATION; TRANSITION RULE.**—

(1) **APPLICATION.**—Notwithstanding any provision of section 505A and 505B of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355a, 355c) stating that a provision applies beginning on the date of the enactment of the Best Pharmaceuticals for Children Act of 2007 or the date of the enactment of the Pediatric Research Equity Act of 2007, any amendment made by this Act to such a provision applies beginning on the date of the enactment of this Act.

(2) **TRANSITIONAL RULE FOR ADVERSE EVENT REPORTING.**—With respect to a drug for which a labeling change described under section 505A(l)(1) or 505B(i)(1) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355a(l)(1); 355c(i)(1)) is approved or made, respectively, during the one-year period that ends on the day before the date of enactment of this Act, the Secretary shall apply section 505A(l) and section 505B(i), as applicable, to such drug, as such sections were in effect on such day.

SEC. 510. PEDIATRIC RARE DISEASES.

(a) **PUBLIC MEETING.**—Not later than 18 months after the date of enactment of this Act, the Secretary shall hold at least one public meeting to discuss ways to encourage and accelerate the development of new therapies for pediatric rare diseases.

(b) **REPORT.**—Not later than 180 days after the date of the public meeting under subsection (a), the Secretary shall issue a report that includes a strategic plan for encouraging and accelerating the development of new therapies for treating pediatric rare diseases.

Pediatric Advisory Committee

Sec. 14 of the Best Pharmaceuticals for Children Act [42 U.S.C. 284m note]

SEC. 14. PEDIATRIC ADVISORY COMMITTEE.

(a) IN GENERAL.—The Secretary of Health and Human Services shall, under section 222 of the Public Health Service Act (42 U.S.C. 217a) or other appropriate authority, convene and consult an advisory committee on pediatric therapeutics (including drugs and biological products) and medical devices (referred to in this section as the ‘advisory committee’).

(b) PURPOSE.—

(1) IN GENERAL.—The advisory committee shall advise and make recommendations to the Secretary, through the Commissioner of Food and Drugs, on matters relating to pediatric therapeutics (including drugs and biological products) and medical devices.

(2) MATTERS INCLUDED.—The matters referred to in paragraph (1) include—

(A) pediatric research conducted under sections 351, 409I, and 499 of the Public Health Service Act and sections 501, 502, 505, 505A, 505B, 510(k), 515, and 520(m) of the Federal Food, Drug, and Cosmetic Act;

(B) identification of research priorities related to therapeutics (including drugs and biological products) and medical devices for pediatric populations and the need for additional diagnostics and treatments for specific pediatric diseases or conditions;

(C) the ethics, design, and analysis of clinical trials related to pediatric therapeutics (including drugs and biological products) and medical devices.

(c) COMPOSITION.—The advisory committee shall include representatives of pediatric health organizations, pediatric researchers, relevant patient and patient-family organizations, and other experts selected by the Secretary.

(d) Notwithstanding section 14 of the Federal Advisory Committee Act, the advisory committee shall continue to operate to carry out the advisory committee’s responsibilities under sections 505A, 505B, and 520(m) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355a, 355c, and 360j(m)).

Pediatric Subcommittee of the Oncologic Drugs Advisory Committee

Sec. 15 of the Best Pharmaceuticals for Children Act (PL 107-109), as amended by the Food and Drug Administration Amendments Act of 2007 (110-85)

SEC. 15. PEDIATRIC SUBCOMMITTEE OF THE ONCOLOGIC DRUGS ADVISORY COMMITTEE.

(a) CLARIFICATION OF AUTHORITIES.—

(1) IN GENERAL.—The Pediatric Subcommittee of the Oncologic Drugs Advisory Committee (referred to in this section as the “Subcommittee”), in carrying out the mission of reviewing and evaluating the data concerning the safety and effectiveness of marketed and investigational human drug products for use in the treatment of pediatric cancers, shall—

(A) evaluate and, to the extent practicable, prioritize new and emerging therapeutic alternatives available to treat pediatric cancer;

(B) provide recommendations and guidance to help ensure that children with cancer have timely access to the most promising new cancer therapies;

(C) advise on ways to improve consistency in the availability of new therapeutic agents; and

(D) provide recommendations to the internal review committee created under section 505C of the Federal Food, Drug, and Cosmetic Act regarding the implementation of amendments to sections 505A and 505B of the Federal Food, Drug, and Cosmetic Act with respect to the treatment of pediatric cancers.

(2) MEMBERSHIP.—

(A) IN GENERAL.—The Secretary shall appoint not more than 11 voting members to the Pediatric Subcommittee from the membership of the Pediatric Pharmacology Advisory Committee and the Oncologic Drugs Advisory Committee.

(B) REQUEST FOR PARTICIPATION.—The Subcommittee shall request participation of the following members in the scientific and ethical

consideration of topics of pediatric cancer, as necessary:

- (i) At least two pediatric oncology specialists from the National Cancer Institute.
- (ii) At least four pediatric oncology specialists from—
 - (I) the Children's Oncology Group;
 - (II) other pediatric experts with an established history of conducting clinical trials in children; or
 - (III) consortia sponsored by the National Cancer Institute, such as the Pediatric Brain Tumor Consortium, the New Approaches to Neuroblastoma Therapy or other pediatric oncology consortia.
- (iii) At least two representatives of the pediatric cancer patient and patient-family community.
- (iv) One representative of the nursing community.
- (v) At least one statistician.
- (vi) At least one representative of the pharmaceutical industry.

(3) CONTINUATION OF OPERATION OF SUBCOMMITTEE.—Notwithstanding section 14 of the Federal Advisory Committee Act, the Subcommittee shall continue to operate for the duration of the operation of the Oncologic Drugs Advisory Committee .

...

(d) REPORT.—Not later than January 31, 2009, the Secretary of Health and Human Services, acting through the Commissioner of Food and Drugs and in consultation with the Director of the National Institutes of Health, shall submit to the Committee on Health, Education, Labor, and Pensions of the Senate and the Committee on Energy and Commerce of the House of Representatives a report on patient access to new therapeutic agents for pediatric cancer, including access to single patient use of new therapeutic agents.

Foundation for the National Institutes of Health
Sec. 499(c) of the Public Health Service Act [42 U.S.C. 290b(c)]

(c) CERTAIN ACTIVITIES OF FOUNDATION.—

(1) IN GENERAL.—In carrying out subsection (b) of this section, the Foundation may solicit and accept gifts, grants, and other donations, establish accounts, and invest and expend funds in support of the following activities with respect to the purpose described in such subsection:

...

(C) A program to collect funds for pediatric pharmacologic research and studies.

Humanitarian Device Exemption (HDE)
Sec. 520(m) of the Federal Food, Drug and Cosmetic Act [42 U.S.C. 360j(m)]

(m) HUMANITARIAN DEVICE EXEMPTION.—

(1) To the extent consistent with the protection of the public health and safety and with ethical standards, it is the purpose of this subsection to encourage the discovery and use of devices intended to benefit patients in the treatment and diagnosis of diseases or conditions that affect fewer than 4,000 individuals in the United States.

(2) The Secretary may grant a request for an exemption from the effectiveness requirements of sections 514 and 515 for a device for which the Secretary finds that—

- (A) the device is designed to treat or diagnose a disease or condition that affects fewer than 4,000 individuals in the United States,
- (B) the device would not be available to a person with a disease or condition referred to in subparagraph (A) unless the Secretary grants such an exemption and there is no comparable device, other than under this exemption, available to treat or diagnose such disease or condition, and
- (C) the device will not expose patients to an unreasonable or significant risk of illness or injury and the probable benefit to health from

the use of the device outweighs the risk of injury or illness from its use, taking into account the probable risks and benefits of currently available devices or alternative forms of treatment.

The request shall be in the form of an application submitted to the Secretary and such application shall include the certification required under section 402(i)(5)(B) of the Public Health Service Act (which shall not be considered an element of such application). Not later than 75 days after the date of the receipt of the application, the Secretary shall issue an order approving or denying the application.

(3) Except as provided in paragraph (6), no person granted an exemption under paragraph (2) with respect to a device may sell the device for an amount that exceeds the costs of research and development, fabrication, and distribution of the device.

(4) Devices granted an exemption under paragraph (2) may only be used—

(A) in facilities that have established, in accordance with regulations of the Secretary, a local institutional review committee to supervise clinical testing of devices in the facilities, and

(B) if, before the use of a device, an institutional review committee approves the use in the treatment or diagnosis of a disease or condition referred to in paragraph (2)(A), unless a physician determines in an emergency situation that approval from a local institutional review committee can not be obtained in time to prevent serious harm or death to a patient.

In a case described in subparagraph (B) in which a physician uses a device without an approval from an institutional review committee, the physician shall, after the use of the device, notify the chairperson of the local institutional review committee of such use. Such notification shall include the identification of the patient involved, the date on which the device was used, and the reason for the use.

(5) The Secretary may require a person granted an exemption under paragraph (2) to demonstrate continued compliance with the requirements of this subsection if the Secretary believes such demonstration to be necessary to protect the public health, if the Secretary has reason to believe that the requirements of paragraph (6) are no longer met, or if the Secretary has reason to believe that the criteria for the exemption are no longer met. If the person granted an exemption under paragraph (2) fails to demonstrate continued compliance with the requirements of this subsection, the Secretary may suspend or withdraw the exemption from the effectiveness requirements of sections 514 and 515 for a humanitarian device only after providing notice and an opportunity for an informal hearing.

(6)

(A) Except as provided in subparagraph (D), the prohibition in paragraph (3) shall not apply with respect to a person granted an exemption under paragraph (2) if each of the following conditions apply:

(i) The device with respect to which the exemption is granted—

(I) is intended for the treatment or diagnosis of a disease or condition that occurs in pediatric patients or in a pediatric subpopulation, and such device is labeled for use in pediatric patients or in a pediatric subpopulation in which the disease or condition occurs; or

(II) is intended for the treatment or diagnosis of a disease or condition that does not occur in pediatric patients or that occurs in pediatric patients in such numbers that the development of the device for such patients is impossible, highly impracticable, or unsafe.

(ii) During any calendar year, the number of such devices distributed during that year under each exemption granted under this subsection does not exceed the annual distribution number for such device. In this paragraph, the term 'annual distribution number' means the number of such devices reasonably needed to treat, diagnose, or cure a population of 4,000 individuals in the United States. The Secretary shall determine the annual distribution number when the Secretary grants such exemption.

(iii) Such person immediately notifies the Secretary if the number of such devices distributed during any calendar year exceeds the annual distribution number referred to in clause (ii).

(iv) The request for such exemption is submitted on or before October 1, 2017.

(B) The Secretary may inspect the records relating to the number of devices distributed during any calendar year of a person granted an exemption under paragraph (2) for which the prohibition in paragraph (3) does not apply.

(C) A person may petition the Secretary to modify the annual distribution number determined by the Secretary under subparagraph (A)(ii) with respect to a device if additional information arises, and the Secretary may modify such annual distribution number.

(D) If a person notifies the Secretary, or the Secretary determines through an inspection under subparagraph (B), that the number of devices distributed during any calendar year exceeds the annual distribution number, as required under subparagraph (A)(iii), and modified under subparagraph (C), if applicable, then the prohibition in paragraph (3) shall apply with respect to such person for such device for any sales of such device after such notification.

(E)

(i) In this subsection, the term "pediatric patients" means patients who are 21 years of age or younger at the time of the diagnosis or treatment.

(ii) In this subsection, the term "pediatric subpopulation" means 1 of the following populations:

(I) Neonates.

(II) Infants.

(III) Children.

(IV) Adolescents.

(7) The Secretary shall refer any report of an adverse event regarding a device described in paragraph (6)(A)(i)(I) for which the prohibition under paragraph (3) does not apply pursuant to paragraph (6)(A) that the Secretary receives to the Office of Pediatric Therapeutics, established under section 6 of the Best Pharmaceuticals for Children Act. In considering the report, the Director of the Office of Pediatric Therapeutics, in consultation with experts in the Center for Devices and Radiological Health, shall provide for periodic review of the report by the Pediatric Advisory Committee, including obtaining any recommendations of such committee regarding whether the Secretary should take action under this chapter in response to the report.

(8) The Secretary, acting through the Office of Pediatric Therapeutics and the Center for Devices and Radiological Health, shall provide for an annual review by the Pediatric Advisory Committee of all devices described in paragraph (6)(A)(i)(I) to ensure that the exemption under paragraph (2) remains appropriate for the pediatric populations for which it is granted.

Other Device Provisions

Food and Drug Administration Safety and Innovation Act (PL 112-144)

SEC. 613. HUMANITARIAN DEVICE EXEMPTIONS.

(b) APPLICABILITY TO EXISTING DEVICES.—A sponsor of a device for which an exemption was approved under paragraph (2) of section 520(m) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360j(m)) before the date of enactment of this Act may seek a determination under subclause (I) or (II) of section 520(m)(6)(A)(i) (as amended by subsection (a)). If the Secretary of Health and Human Services determines that such subclause (I) or (II) applies with respect to a device, clauses (ii), (iii), and (iv) of subparagraph (A) and subparagraphs (B), (C), (D), and (E) of paragraph (6) of such section 520(m) shall apply to such device, and the Secretary shall determine the annual distribution number for purposes of clause (ii) of such subparagraph (A) when making the determination under this subsection.

SEC. 620. PEDIATRIC DEVICE CONSORTIA.

(b) FINAL RULE RELATING TO TRACKING OF PEDIATRIC USES OF DEVICES.—The Secretary of Health and Human Services shall issue—

(1) a proposed rule implementing section 515A(a)(2) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360e-1(a)(2)) not later than December 31, 2012; and

(2) a final rule implementing such section not later than December 31, 2013.

Pediatric Device Consortia

Sec. 305 of the Pediatric Medical Device Safety and Improvement Act of 2007 [42 U.S.C. 282 note]

SEC. 305. DEMONSTRATION GRANTS FOR IMPROVING PEDIATRIC DEVICE AVAILABILITY.—

(a) IN GENERAL.—

(1) REQUEST FOR PROPOSALS.—Not later than 90 days after the date of the enactment of this Act, the Secretary of Health and Human Services shall issue a request for proposals for 1 or more grants or contracts to nonprofit consortia for demonstration projects to promote pediatric device development.

(2) DETERMINATION ON GRANTS OR CONTRACTS.—Not later than 180 days after the date the Secretary of Health and Human Services issues a request for proposals under paragraph (1), the Secretary shall make a determination on the grants or contracts under this section.

(b) APPLICATION.—A nonprofit consortium that desires to receive a grant or contract under this section shall submit an application to the

Secretary of Health and Human Services at such time, in such manner, and containing such information as the Secretary may require.

(c) USE OF FUNDS.—A nonprofit consortium that receives a grant or contract under this section shall facilitate the development, production, and distribution of pediatric medical devices by—

- (1) encouraging innovation and connecting qualified individuals with pediatric device ideas with potential manufacturers;
- (2) mentoring and managing pediatric device projects through the development process, including product identification, prototype design, device development, and marketing;
- (3) connecting innovators and physicians to existing Federal and non-Federal resources, including resources from the Food and Drug Administration, the National Institutes of Health, the Small Business Administration, the Department of Energy, the Department of Education, the National Science Foundation, the Department of Veterans Affairs, the Agency for Healthcare Research and Quality, and the National Institute of Standards and Technology;
- (4) assessing the scientific and medical merit of proposed pediatric device projects; and
- (5) providing assistance and advice as needed on business development, personnel training, prototype development, postmarket needs, and other activities consistent with the purposes of this section.

(d) COORDINATION.—

(1) NATIONAL INSTITUTES OF HEALTH.—Each consortium that receives a grant or contract under this section shall—

- (A) coordinate with the National Institutes of Health's pediatric device contact point or office, designated under section 402(b)(23) of the Public Health Service Act, as added by section 304(a) of this Act; and
- (B) provide to the National Institutes of Health any identified pediatric device needs that the consortium lacks sufficient capacity to address or those needs in which the consortium has been unable to stimulate manufacturer interest.

(2) FOOD AND DRUG ADMINISTRATION.—Each consortium that receives a grant or contract under this section shall coordinate with the Commissioner of Food and Drugs and device companies to facilitate the application for approval or clearance of devices labeled for pediatric use.

(3) EFFECTIVENESS AND OUTCOMES.—Each consortium that receives a grant or contract under this section shall annually report to the Secretary of Health and Human Services on the status of pediatric device development, production, and distribution that has been facilitated by the consortium.

(e) AUTHORIZATION OF APPROPRIATIONS.—There are authorized to be appropriated to carry out this section \$5,250,000 for each of fiscal years 2013 through 2017.