110TH CONGRESS
1ST SESSION

# S. 993

To improve pediatric research.

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IN THE SENATE OF THE UNITED STATES

MARCH 27, 2007

Mrs. CLINTON (for herself and Mr. DODD) introduced the following bill; which was read twice and referred to the Committee on Health, Education, Labor, and Pensions

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# A BILL

To improve pediatric research.

*Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled,*

**SECTION 1. SHORT TITLE.**

This Act may be cited as the ''Pediatric Research Improvement Act''.

**SEC. 2. PEDIATRIC FORMULATIONS, EXTRAPOLATIONS, AND DEFERRALS.**

Section 505B(a) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355c(a)) is amended—

(1) in paragraph (4)(C), by adding at the end the following: ''An applicant seeking either a partial

or full 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 website of the Food and Drug Administration'';

(2) in paragraph (2)(B), by adding at the end the following:

''(iii) INFORMATION ON EXTRAPOLATION.—A brief documentation of the scientific data supporting the conclusion under clauses (i) and (ii) shall be included in the medical review that is collected as part of the application under section 505 or section 351 of the Public Health Service Act.''; and

(3) by striking paragraph (3) and inserting the following:

''(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 description of the planned or ongoing studies;

''(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) 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.

"(ii) PUBLIC AVAILABILITY.—The information submitted through the annual review under clause (i) shall promptly be made available to the public in an easily accessible manner, including through the website of the Food and Drug Administration.".

**SEC. 3. IMPROVING AVAILABILITY OF PEDIATRIC DATA FOR ALREADY MARKETED PRODUCTS.**

Section 505B(b) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355c(b)) is amended—

(1) by striking paragraph (1) and inserting the following:

''(1) IN GENERAL.—After providing notice in the form of a letter, or a written request under section 505A that was declined by the sponsor or holder, and an opportunity for written response and a meeting, which may include an advisory committee meeting, 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) and the written request, as appropriate, 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) in paragraph (2)(C), by adding at the end the following: ''An applicant seeking either a partial or full 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 website of the Food and Drug Administration.''; and

(3) by striking paragraph (3).

**SEC. 4. REVIEW OF PEDIATRIC ASSESSMENTS; ADVERSE EVENT REPORTING; STRIKE OF SUNSET; LABELING CHANGES; AND PEDIATRIC ASSESSMENTS.**

Section 505B of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355c) is amended—

(1) by striking subsection (h);

(2) by redesignating subsection (f) as subsection (k);

(3) by redesignating subsection (g) as subsection (l); and

(4) by inserting after subsection (e) the following:

''(f) REVIEW OF PEDIATRIC ASSESSMENT REQUESTS, PEDIATRIC ASSESSMENTS, DEFERRALS, AND WAIVERS.—

''(1) REVIEW.—The Secretary shall create an internal committee to review all pediatric assessment requests issued under this section, all pediatric assessments conducted under this section, and all deferral and waiver requests made pursuant to this section. Such internal committee shall include individuals with the following expertise:

''(A) Pediatrics.

''(B) Biopharmacology.

''(C) Statistics.

''(D) Drugs and drug formulations.

''(E) Pediatric ethics.

''(F) Legal issues.

''(G) Appropriate expertise pertaining to the pediatric product under review.

''(H) 1 or more experts from the Office of Pediatric Therapeutics.

''(I) Other individuals as designated by the Secretary.

''(2) REVIEW OF REQUESTS FOR PEDIATRIC ASSESSMENTS, DEFERRALS, AND WAIVERS.—All written requests for a pediatric assessment issued pursuant to this section and all requests for deferrals and waivers from the requirement to conduct a pediatric assessment under this section shall be reviewed and approved by the committee established under paragraph (1).

''(3) REVIEW OF ASSESSMENTS.—The committee established under paragraph (1) shall review all assessments conducted under this section to determine whether such assessments meet the requirements of this section.

''(4) TRACKING OF ASSESSMENTS AND LABELING CHANGES.—The committee established under paragraph (1) is responsible for tracking and making public in an easily accessible manner, including through posting on the website of the Food and Drug Administration—

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

''(B) the specific drugs and drug 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) the total number of deferrals requested and granted under this section, and, if granted, the reasons for such deferrals, the timeline for completion, and the number completed and pending by the specified date, as outlined in subsection (a)(3);

''(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 formulations were 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 (i)(2); and

''(I) an annual summary of the information submitted pursuant to subsection (a)(3)(B).

''(g) LABELING CHANGES.—

''(1) PRIORITY STATUS FOR PEDIATRIC SUPPLEMENT.—Any supplement to an application under section 505 and section 351 of the Public Health Service Act proposing a labeling change as a result of any pediatric assessments conducted pursuant to this section—

''(A) shall be considered a priority 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 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—

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

"(ii) if the sponsor does not agree 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, within 30 days after receiving a request under sub-

paragraph (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 Act when a drug lacks appropriate pediatric labeling. Neither course of action (the Pediatric Advisory Committee process of an enforcement action referred to in the preceding sentence) shall preclude, delay, or serve as the basis to stay the other course of action.

''(3) OTHER LABELING CHANGES.—If the Secretary makes a determination that a pediatric assessment conducted under this section does not demonstrate that the drug that is the subject of such assessment is safe and effective, the Secretary shall order the label 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 180 days after the date of submission of a pediatric assessment under this section, the Commissioner 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 website of the Food and Drug Administration.

''(2) DISSEMINATION OF INFORMATION REGARDING LABELING CHANGES.—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)(4)(H) distribute such information to physicians and other health care providers.

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

''(i) ADVERSE EVENT REPORTING.—

''(1) REPORTING IN YEAR 1.—During the 1-year 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 the report, the Director of such Office shall provide for the 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 Act in response to such report.

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

**SEC. 5. MEANINGFUL THERAPEUTIC BENEFIT.**

Section 505B(c) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355c) is amended—

(1) by striking ''estimates'' and inserting ''determines''; and

(2) by striking ''would'' and inserting ''could''.

**SEC. 6. REPORTS.**

(a) IOM STUDY.—Section 505B of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355c), as amended by section 4, is further amended by adding after subsection (l), the following:

''(m) INSTITUTE OF MEDICINE STUDY.—

''(1) IN GENERAL.—Not later than 3 years after the date of enactment of the Pediatric Research Improvement Act, 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 since 1997.

''(2) CONTENT OF STUDY.—The study under paragraph (1) shall review and assess—

''(A) pediatric studies conducted pursuant to this section since 1997 and labeling changes made as a result of such studies; and

''(B) the use of extrapolation for pediatric subpopulations, the use of alternative endpoints for pediatric populations, neonatal assessment tools, 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 and the Center for Biologics Evaluation and Research in order to make the required assessment.''.

(b) PREA REPORT.—The Pediatric Research Equity Act of 2003 (Public Law 108–155) is amended by adding at the end the following:

**''SEC. 5. REPORT.**

''Not later than September 1, 2010, the Comptroller General of the United States, in consultation with the Secretary of Health and Human Services, shall submit to Congress a report that addresses the effectiveness of section 505B of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355a) in ensuring that medicines used by children are tested and properly labeled, including—

''(1) the number and importance of drugs for children that are being tested as a result of this provision and the importance for children, health care providers, parents, and others of labeling changes made as a result of such testing;

''(2) the number and importance of drugs for children that are not being tested for their use not-

withstanding the provisions of this Act, and possible reasons for the lack of testing; and

''(3) the number of drugs for which testing is being done and labeling changes required, including the date labeling changes are made and which labeling changes required the use of the dispute resolution process established pursuant to the amendments made by this Act, together with a description of the outcomes of such process, including a description of the disputes and the recommendations of the Pediatric Advisory Committee.''.

**SEC. 7. TECHNICAL CORRECTIONS.**

Section 505B(a)(2)(B)(ii) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355c(a)(2)(B)(ii)) is amended by striking ''one'' and inserting ''1''.

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