# Calendar No. 183

108TH CONGRESS
1ST SESSION

# S. 650

**[Report No. 108–84]**

To amend the Federal Food, Drug, and Cosmetic Act to authorize the Food and Drug Administration to require certain research into drugs used in pediatric patients.

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IN THE SENATE OF THE UNITED STATES

MARCH 18, 2003

Mr. DEWINE (for himself, Mrs. CLINTON, Mr. GREGG, Mr. DODD, Mr. KENNEDY, Mrs. MURRAY, and Mr. FRIST) introduced the following bill; which was referred to the Committee on Health, Education, Labor, and Pensions

JUNE 27 (legislative day, JUNE 26), 2003

Reported by Mr. GREGG, with an amendment

[Omit the part struck through and insert the part printed in italic]

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# A BILL

To amend the Federal Food, Drug, and Cosmetic Act to authorize the Food and Drug Administration to require certain research into drugs used in pediatric patients.

*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 Equity Act of 2003''.

**SEC. 2. RESEARCH INTO PEDIATRIC USES FOR DRUGS AND BIOLOGICAL PRODUCTS.**

(a) IN GENERAL.—Subchapter A of chapter V of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 351 et seq.) is amended by inserting after section 505A the following:

**''SEC. 505B. RESEARCH INTO PEDIATRIC USES FOR DRUGS AND BIOLOGICAL PRODUCTS.**

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

''(1) IN GENERAL.—A person that submits an application (or supplement to an application)—

''(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 1 age group can be extrapolated to another age group.

''(3) DEFERRAL.—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—

''(A) 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

''(B) the applicant submits to the Secretary—

''(i) certification of the grounds for deferring the assessments;

"(ii) a description of the planned or ongoing studies; and

"(iii) evidence that the studies are being conducted or will be conducted with due diligence and at the earliest possible time.

"(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 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.

"(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.—After providing notice in the form of a letter 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 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) the absence of adequate labeling could pose significant risks to pediatric patients; or

''(B)(i) 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; and

''(ii) the absence of adequate labeling could pose significant risks 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 for-

mulation, the waiver shall cover only the pediatric groups requiring that formulation.

"(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) RELATIONSHIP TO OTHER PEDIATRIC PROVISIONS.—

"(A) NO ASSESSMENT WITHOUT WRITTEN REQUEST.—No assessment may be required under paragraph (1) for a drug subject to an approved application under section 505 unless—

"(i) the Secretary has issued a written request for a related pediatric study under section 505A(c) of this Act or section 409I of the Public Health Service Act (42 U.S.C. 284m);

"(ii)(I) if the request was made under section 505A(c)—

''(aa) the recipient of the written request does not agree to the request; or

''(bb) the Secretary does not receive a response as specified under section 505A(d)(4)(A); or

''(II) if the request was made under section 409I of the Public Health Service Act (42 U.S.C. 284m)—

''(aa) the recipient of the written request does not agree to the request; or

''(bb) the Secretary does not receive a response as specified under section 409I(c)(2) of that Act; and

''(iii)(I) the Secretary certifies under subparagraph (B) that there are insufficient funds under sections 409I and 499 of the Public Health Service Act (42 U.S.C. 284m, 290b) to conduct the study; or

''(II) the Secretary publishes in the Federal Register a certification that certifies that—

''(aa) no contract or grant has been awarded under section 409I or

499 of the Public Health Service Act (42 U.S.C. 284m, 290b); and

"(bb) not less than 270 days have passed since the date of a certification under subparagraph (B) that there are sufficient funds to conduct the study.

"(B) NO AGREEMENT TO REQUEST.—Not later than 60 days after determining that no holder will agree to the written request (including a determination that the Secretary has not received a response specified under section 505A(d) of this Act or section 409I of the Public Health Service Act (42 U.S.C. 284m), the Secretary shall certify whether the Secretary has sufficient funds to conduct the study under section 409I or 499 of the Public Health Service Act (42 U.S.C. 284m, 290b), taking into account the prioritization under section 409I.

"(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)(i) 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 estimates that—

''(1) if approved, the drug or biological product would represent a significant improvement in the treatment, diagnosis, or prevention of a disease, compared with marketed products adequately labeled for that use in the relevant pediatric population; or

''(2) the drug or biological product is in a class of products or for an indication for which there is a need for additional options.

''(d) SUBMISSION OF ASSESSMENTS.—If a person fails to submit an assessment described in subsection (a)(2), or a request for approval of a pediatric formulation described in subsection (a) or (b), in accordance with applicable provisions of subsections (a) and (b)—

''(1) the drug or biological product that is the subject of the assessment or request may be considered misbranded and subject to relevant enforcement action (except that the drug or biological product shall not be subject to action under section 303); but

''(2) the failure to submit the assessment or request 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 (42 U.S.C. 262).

''(e) MEETINGS.—Before and during the investigational process for a new drug or biological product, the Secretary shall meet at appropriate times with the sponsor of the new drug or biological product to discuss—

''(1) information that the sponsor submits on plans and timelines for pediatric studies; or

''(2) any planned request by the sponsor for waiver or deferral of pediatric studies.

''(f) 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.

''(g) 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.''.~~ *526.*

*''(h) INTEGRATION WITH OTHER PEDIATRIC STUDIES.—The authority under this section shall remain in effect so long as an application subject to this section may*

*be accepted for filing by the Secretary on or before the date specified in section 505A(n).''.*

(b) CONFORMING AMENDMENTS.—

(1) Section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(b)(1)) is amended in the second sentence—

(A) by striking ''and (F)'' and inserting ''(F)''; and

(B) by striking the period at the end and inserting '', and (G) any assessments required under section 505B.''.

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

(A) in the subsection heading, by striking ''REGULATIONS'' and inserting ''PEDIATRIC RESEARCH REQUIREMENTS''; and

(B) by striking ''pursuant to regulations promulgated by the Secretary'' and inserting ''by a provision of law (including a regulation) other than this section''.

(3) Section 351(a)(2) of the Public Health Service Act (42 U.S.C. 262(a)(2)) is amended—

(A) by redesignating subparagraph (B) as subparagraph (C); and

(B) by inserting after subparagraph (A) the following:

''(B) PEDIATRIC STUDIES.—A person that submits an application for a license under this paragraph shall submit to the Secretary as part of the application any assessments required under section 505B of the Federal Food, Drug, and Cosmetic Act.''.

**SEC. 3. TECHNICAL AND CONFORMING AMENDMENTS.**

(a) ABBREVIATED NEW DRUG APPLICATION.—Section 505A of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355a) is amended in subparagraphs (A) and (B) of subsection (b)(2) and subparagraphs (A) and (B) of subsection (c)(2) by striking ''505(j)(4)(B)'' and inserting ''505(j)(5)(B)''.

(b) PEDIATRIC ADVISORY COMMITTEE.—

(1) Section 505A(i)(2) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355a(i)(2)) is amended by striking ''Advisory Subcommittee of the Anti-Infective Drugs'' each place it appears.

(2) Section 14 of the Best Pharmaceuticals for Children Act (42 U.S.C. 284m note; Public Law 107–109) is amended—

(A) in the section heading, by striking ''**PHARMACOLOGY**'';

(B) in subsection (a), by striking ''(42 U.S.C. 217a),'' and inserting (42 U.S.C. 217a) or other appropriate authority,'';

(C) in subsection (b)—

(i) in paragraph (1), by striking ''and in consultation with the Director of the National Institutes of Health''; and

(ii) in paragraph (2), by striking ''and 505A'' and inserting ''505A, and 505B''; and

(D) by striking ''pharmacology'' each place it appears and inserting ''therapeutics''.

(3) Section 15(a)(2)(A) of the Best Pharmaceuticals for Children Act (115 Stat. 1419) is amended by striking ''Pharmacology''.

(4) Section 16(1)(C) of the Best Pharmaceuticals for Children Act (21 U.S.C. 355a note; Public Law 107–109) is amended by striking ''Advisory Subcommittee of the Anti-Infective Drugs''.

(5) Section 17(b)(1) of the Best Pharmaceuticals for Children Act (21 U.S.C. 355b(b)(1)) is amended in the second sentence by striking ''Advisory Subcommittee of the Anti-Infective Drugs''.

(6) Paragraphs (8), (9), and (11) of section 409I(c) of the Public Health Service Act (42 U.S.C.

284m(c)) are amended by striking ''Advisory Subcommittee of the Anti-Infective Drugs'' each place it appears.

**SEC. 4. EFFECTIVE DATE.**

(a) IN GENERAL.—This Act and the amendments made by this Act take effect October 17, 2002.

(b) NO LIMITATION OF AUTHORITY.—Neither the lack of guidance or regulations to implement this Act or the amendments made by this Act nor the pendency of the process for issuing guidance or regulations shall limit the authority of the Secretary of Health and Human Services under, or defer any requirement under, this Act or those amendments.

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Reported with an amendment