

**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.

1       *Be it enacted by the Senate and House of Representa-*  
2       *tives of the United States of America in Congress assembled,*

1 **SECTION 1. SHORT TITLE.**

2       This Act may be cited as the “Pediatric Research Eq-  
3 uity Act of 2003”.

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

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

10 **“SEC. 505B. RESEARCH INTO PEDIATRIC USES FOR DRUGS**  
11 **AND BIOLOGICAL PRODUCTS.**

12       “(a) NEW DRUGS AND BIOLOGICAL PRODUCTS.—

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

15                       “(A) under section 505 for a new active in-  
16 gredient, new indication, new dosage form, new  
17 dosing regimen, or new route of administration;  
18 or

19                       “(B) under section 351 of the Public  
20 Health Service Act (42 U.S.C. 262) for a new  
21 active ingredient, new indication, new dosage  
22 form, new dosing regimen, or new route of ad-  
23 ministration;

24 shall submit with the application the assessments de-  
25 scribed in paragraph (2).

26       “(2) ASSESSMENTS.—

1           “(A) IN GENERAL.—The assessments re-  
2           ferred to in paragraph (1) shall contain data,  
3           gathered using appropriate formulations for  
4           each age group for which the assessment is re-  
5           quired, that are adequate—

6                   “(i) to assess the safety and effective-  
7                   ness of the drug or the biological product  
8                   for the claimed indications in all relevant  
9                   pediatric subpopulations; and

10                   “(ii) to support dosing and adminis-  
11                   tration for each pediatric subpopulation for  
12                   which the drug or the biological product is  
13                   safe and effective.

14           “(B) SIMILAR COURSE OF DISEASE OR  
15           SIMILAR EFFECT OF DRUG OR BIOLOGICAL  
16           PRODUCT.—

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

1 “(ii) EXTRAPOLATION BETWEEN AGE  
 2 GROUPS.—A study may not be needed in  
 3 each pediatric age group if data from 1  
 4 age group can be extrapolated to another  
 5 age group.

6 “(3) DEFERRAL.—On the initiative of the Sec-  
 7 retary or at the request of the applicant, the Sec-  
 8 retary may defer submission of some or all assess-  
 9 ments required under paragraph (1) until a specified  
 10 date after approval of the drug or issuance of the li-  
 11 cense for a biological product if—

12 “(A) the Secretary finds that—

13 “(i) the drug or biological product is  
 14 ready for approval for use in adults before  
 15 pediatric studies are complete;

16 “(ii) pediatric studies should be de-  
 17 layed until additional safety or effective-  
 18 ness data have been collected; or

19 “(iii) there is another appropriate rea-  
 20 son for deferral; and

21 “(B) the applicant submits to the Sec-  
 22 retary—

23 “(i) certification of the grounds for  
 24 deferring the assessments;

1 “(ii) a description of the planned or  
2 ongoing studies; and

3 “(iii) evidence that the studies are  
4 being conducted or will be conducted with  
5 due diligence and at the earliest possible  
6 time.

7 “(4) WAIVERS.—

8 “(A) FULL WAIVER.—On the initiative of  
9 the Secretary or at the request of an applicant,  
10 the Secretary shall grant a full waiver, as ap-  
11 propriate, of the requirement to submit assess-  
12 ments for a drug or biological product under  
13 this subsection if the applicant certifies and the  
14 Secretary finds that—

15 “(i) necessary studies are impossible  
16 or highly impracticable (because, for exam-  
17 ple, the number of patients is so small or  
18 the patients are geographically dispersed);

19 “(ii) there is evidence strongly sug-  
20 gesting that the drug or biological product  
21 would be ineffective or unsafe in all pedi-  
22 atric age groups; or

23 “(iii) the drug or biological product—

1 “(I) does not represent a mean-  
2 ingful therapeutic benefit over existing  
3 therapies for pediatric patients; and

4 “(II) is not likely to be used in a  
5 substantial number of pediatric pa-  
6 tients.

7 “(B) PARTIAL WAIVER.—On the initiative  
8 of the Secretary or at the request of an appli-  
9 cant, the Secretary shall grant a partial waiver,  
10 as appropriate, of the requirement to submit as-  
11 sessments for a drug or biological product  
12 under this subsection with respect to a specific  
13 pediatric age group if the applicant certifies  
14 and the Secretary finds that—

15 “(i) necessary studies are impossible  
16 or highly impracticable (because, for exam-  
17 ple, the number of patients in that age  
18 group is so small or patients in that age  
19 group are geographically dispersed);

20 “(ii) there is evidence strongly sug-  
21 gesting that the drug or biological product  
22 would be ineffective or unsafe in that age  
23 group;

24 “(iii) the drug or biological product—

1 “(I) does not represent a mean-  
 2 ingful therapeutic benefit over existing  
 3 therapies for pediatric patients in that  
 4 age group; and

5 “(II) is not likely to be used by  
 6 a substantial number of pediatric pa-  
 7 tients in that age group; or

8 “(iv) the applicant can demonstrate  
 9 that reasonable attempts to produce a pe-  
 10 diatric formulation necessary for that age  
 11 group have failed.

12 “(C) PEDIATRIC FORMULATION NOT POS-  
 13 SIBLE.—If a waiver is granted on the ground  
 14 that it is not possible to develop a pediatric for-  
 15 mulation, the waiver shall cover only the pedi-  
 16 atric groups requiring that formulation.

17 “(D) LABELING REQUIREMENT.—If the  
 18 Secretary grants a full or partial waiver because  
 19 there is evidence that a drug or biological prod-  
 20 uct would be ineffective or unsafe in pediatric  
 21 populations, the information shall be included  
 22 in the labeling for the drug or biological prod-  
 23 uct.

24 “(b) MARKETED DRUGS AND BIOLOGICAL PROD-  
 25 UCTS.—

1           “(1) IN GENERAL.—After providing notice in  
 2           the form of a letter and an opportunity for written  
 3           response and a meeting, which may include an advisory  
 4           committee meeting, the Secretary may (by  
 5           order in the form of a letter) require the holder of  
 6           an approved application for a drug under section  
 7           505 or the holder of a license for a biological product  
 8           under section 351 of the Public Health Service  
 9           Act (42 U.S.C. 262) to submit by a specified date  
 10          the assessments described in subsection (a)(2) if the  
 11          Secretary finds that—

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

15                 “(ii) the absence of adequate labeling could  
 16                 pose significant risks to pediatric patients; or

17                 “(B)(i) there is reason to believe that the  
 18                 drug or biological product would represent a  
 19                 meaningful therapeutic benefit over existing  
 20                 therapies for pediatric patients for 1 or more of  
 21                 the claimed indications; and

22                 “(ii) the absence of adequate labeling could  
 23                 pose significant risks to pediatric patients.

24          “(2) WAIVERS.—

1           “(A) FULL WAIVER.—At the request of an  
2           applicant, the Secretary shall grant a full waiv-  
3           er, as appropriate, of the requirement to submit  
4           assessments under this subsection if the appli-  
5           cant certifies and the Secretary finds that—

6                   “(i) necessary studies are impossible  
7                   or highly impracticable (because, for exam-  
8                   ple, the number of patients in that age  
9                   group is so small or patients in that age  
10                  group are geographically dispersed); or

11                  “(ii) there is evidence strongly sug-  
12                  gesting that the drug or biological product  
13                  would be ineffective or unsafe in all pedi-  
14                  atric age groups.

15           “(B) PARTIAL WAIVER.—At the request of  
16           an applicant, the Secretary shall grant a partial  
17           waiver, as appropriate, of the requirement to  
18           submit assessments under this subsection with  
19           respect to a specific pediatric age group if the  
20           applicant certifies and the Secretary finds  
21           that—

22                   “(i) necessary studies are impossible  
23                   or highly impracticable (because, for exam-  
24                   ple, the number of patients in that age

1 group is so small or patients in that age  
2 group are geographically dispersed);

3 “(ii) there is evidence strongly sug-  
4 gesting that the drug or biological product  
5 would be ineffective or unsafe in that age  
6 group;

7 “(iii)(I) the drug or biological prod-  
8 uct—

9 “(aa) does not represent a mean-  
10 ingful therapeutic benefit over existing  
11 therapies for pediatric patients in that  
12 age group; and

13 “(bb) is not likely to be used in  
14 a substantial number of pediatric pa-  
15 tients in that age group; and

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

19 “(iv) the applicant can demonstrate  
20 that reasonable attempts to produce a pe-  
21 diatric formulation necessary for that age  
22 group have failed.

23 “(C) PEDIATRIC FORMULATION NOT POS-  
24 SIBLE.—If a waiver is granted on the ground  
25 that it is not possible to develop a pediatric for-

1           mulation, the waiver shall cover only the pedi-  
2           atric groups requiring that formulation.

3           “(D) LABELING REQUIREMENT.—If the  
4           Secretary grants a full or partial waiver because  
5           there is evidence that a drug or biological prod-  
6           uct would be ineffective or unsafe in pediatric  
7           populations, the information shall be included  
8           in the labeling for the drug or biological prod-  
9           uct.

10          “(3) RELATIONSHIP TO OTHER PEDIATRIC PRO-  
11          VISIONS.—

12               “(A) NO ASSESSMENT WITHOUT WRITTEN  
13               REQUEST.—No assessment may be required  
14               under paragraph (1) for a drug subject to an  
15               approved application under section 505 un-  
16               less—

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

22                       “(ii)(I) if the request was made under  
23                       section 505A(c)—

1 “(aa) the recipient of the written  
2 request does not agree to the request;  
3 or

4 “(bb) the Secretary does not re-  
5 ceive a response as specified under  
6 section 505A(d)(4)(A); or

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

10 “(aa) the recipient of the written  
11 request does not agree to the request;  
12 or

13 “(bb) the Secretary does not re-  
14 ceive a response as specified under  
15 section 409I(c)(2) of that Act; and

16 “(iii)(I) the Secretary certifies under  
17 subparagraph (B) that there are insuffi-  
18 cient funds under sections 409I and 499 of  
19 the Public Health Service Act (42 U.S.C.  
20 284m, 290b) to conduct the study; or

21 “(II) the Secretary publishes in the  
22 Federal Register a certification that cer-  
23 tifies that—

24 “(aa) no contract or grant has  
25 been awarded under section 409I or

1 499 of the Public Health Service Act  
2 (42 U.S.C. 284m, 290b); and

3 “(bb) not less than 270 days  
4 have passed since the date of a certifi-  
5 cation under subparagraph (B) that  
6 there are sufficient funds to conduct  
7 the study.

8 “(B) NO AGREEMENT TO REQUEST.—Not  
9 later than 60 days after determining that no  
10 holder will agree to the written request (includ-  
11 ing a determination that the Secretary has not  
12 received a response specified under section  
13 505A(d) of this Act or section 409I of the Pub-  
14 lic Health Service Act (42 U.S.C. 284m), the  
15 Secretary shall certify whether the Secretary  
16 has sufficient funds to conduct the study under  
17 section 409I or 499 of the Public Health Serv-  
18 ice Act (42 U.S.C. 284m, 290b), taking into ac-  
19 count the prioritization under section 409I.

20 “(c) MEANINGFUL THERAPEUTIC BENEFIT.—For  
21 the purposes of paragraph (4)(A)(iii)(I) and (4)(B)(iii)(I)  
22 of subsection (a) and paragraphs (1)(B)(i) and  
23 (2)(B)(iii)(I)(aa) of subsection (b), a drug or biological  
24 product shall be considered to represent a meaningful

1 therapeutic benefit over existing therapies if the Secretary  
2 estimates that—

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

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

11 “(d) SUBMISSION OF ASSESSMENTS.—If a person  
12 fails to submit an assessment described in subsection  
13 (a)(2), or a request for approval of a pediatric formulation  
14 described in subsection (a) or (b), in accordance with ap-  
15 plicable provisions of subsections (a) and (b)—

16 “(1) the drug or biological product that is the  
17 subject of the assessment or request may be consid-  
18 ered misbranded and subject to relevant enforcement  
19 action (except that the drug or biological product  
20 shall not be subject to action under section 303); but

21 “(2) the failure to submit the assessment or re-  
22 quest shall not be the basis for a proceeding—

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

1                   “(B) to revoke the license for a biological  
 2                   product under section 351 of the Public Health  
 3                   Service Act (42 U.S.C. 262).

4           “(e) MEETINGS.—Before and during the investiga-  
 5           tional process for a new drug or biological product, the  
 6           Secretary shall meet at appropriate times with the sponsor  
 7           of the new drug or biological product to discuss—

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

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

12           “(f) SCOPE OF AUTHORITY.—Nothing in this section  
 13           provides to the Secretary any authority to require a pedi-  
 14           atric assessment of any drug or biological product, or any  
 15           assessment regarding other populations or uses of a drug  
 16           or biological product, other than the pediatric assessments  
 17           described in this section.

18           “(g) ORPHAN DRUGS.—Unless the Secretary requires  
 19           otherwise by regulation, this section does not apply to any  
 20           drug for an indication for which orphan designation has  
 21           been granted under section ~~526.~~ 526.

22           “(h) *INTEGRATION WITH OTHER PEDIATRIC STUD-*  
 23           *IES.*—*The authority under this section shall remain in ef-*  
 24           *fect so long as an application subject to this section may*

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

3 (b) CONFORMING AMENDMENTS.—

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

7 (A) by striking “and (F)” and inserting  
 8 “(F)”; and

9 (B) by striking the period at the end and  
 10 inserting “, and (G) any assessments required  
 11 under section 505B.”.

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

14 (A) in the subsection heading, by striking  
 15 “REGULATIONS” and inserting “PEDIATRIC RE-  
 16 SEARCH REQUIREMENTS”; and

17 (B) by striking “pursuant to regulations  
 18 promulgated by the Secretary” and inserting  
 19 “by a provision of law (including a regulation)  
 20 other than this section”.

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

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

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

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

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

10 (a) ABBREVIATED NEW DRUG APPLICATION.—Sec-  
 11 tion 505A of the Federal Food, Drug, and Cosmetic Act  
 12 (21 U.S.C. 355a) is amended in subparagraphs (A) and  
 13 (B) of subsection (b)(2) and subparagraphs (A) and (B)  
 14 of subsection (c)(2) by striking “505(j)(4)(B)” and insert-  
 15 ing “505(j)(5)(B)”.

16 (b) PEDIATRIC ADVISORY COMMITTEE.—

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

21 (2) Section 14 of the Best Pharmaceuticals for  
 22 Children Act (42 U.S.C. 284m note; Public Law  
 23 107–109) is amended—

24 (A) in the section heading, by striking  
 25 “**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.

1        284m(c)) are amended by striking “Advisory Sub-  
2        committee of the Anti-Infective Drugs” each place it  
3        appears.

4    **SEC. 4. EFFECTIVE DATE.**

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

7        (b) NO LIMITATION OF AUTHORITY.—Neither the  
8        lack of guidance or regulations to implement this Act or  
9        the amendments made by this Act nor the pendency of  
10       the process for issuing guidance or regulations shall limit  
11       the authority of the Secretary of Health and Human Serv-  
12       ices under, or defer any requirement under, this Act or  
13       those amendments.

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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.

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JUNE 27 (legislative day, JUNE 26), 2003

Reported with an amendment