

108TH CONGRESS
1ST SESSION

S. 650

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.

IN THE SENATE OF THE UNITED STATES

MARCH 18, 2003

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

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,*

3 **SECTION 1. SHORT TITLE.**

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

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

8 (a) IN GENERAL.—Subchapter A of chapter V of the
9 Federal Food, Drug, and Cosmetic Act (21 U.S.C. 351

1 et seq.) is amended by inserting after section 505A the
2 following:

3 **“SEC. 505B. RESEARCH INTO PEDIATRIC USES FOR DRUGS**
4 **AND BIOLOGICAL PRODUCTS.**

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

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

8 “(A) under section 505 for a new active in-
9 gredient, new indication, new dosage form, new
10 dosing regimen, or new route of administration;
11 or

12 “(B) under section 351 of the Public
13 Health Service Act (42 U.S.C. 262) for a new
14 active ingredient, new indication, new dosage
15 form, new dosing regimen, or new route of ad-
16 ministration;

17 shall submit with the application the assessments de-
18 scribed in paragraph (2).

19 “(2) ASSESSMENTS.—

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

1 “(i) to assess the safety and effective-
2 ness of the drug or the biological product
3 for the claimed indications in all relevant
4 pediatric subpopulations; and

5 “(ii) to support dosing and adminis-
6 tration for each pediatric subpopulation for
7 which the drug or the biological product is
8 safe and effective.

9 “(B) SIMILAR COURSE OF DISEASE OR
10 SIMILAR EFFECT OF DRUG OR BIOLOGICAL
11 PRODUCT.—

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

21 “(ii) EXTRAPOLATION BETWEEN AGE
22 GROUPS.—A study may not be needed in
23 each pediatric age group if data from 1
24 age group can be extrapolated to another
25 age group.

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

7 “(A) the Secretary finds that—

8 “(i) the drug or biological product is
9 ready for approval for use in adults before
10 pediatric studies are complete;

11 “(ii) pediatric studies should be de-
12 layed until additional safety or effective-
13 ness data have been collected; or

14 “(iii) there is another appropriate rea-
15 son for deferral; and

16 “(B) the applicant submits to the Sec-
17 retary—

18 “(i) certification of the grounds for
19 deferring the assessments;

20 “(ii) a description of the planned or
21 ongoing studies; and

22 “(iii) evidence that the studies are
23 being conducted or will be conducted with
24 due diligence and at the earliest possible
25 time.

1 “(4) WAIVERS.—

2 “(A) FULL WAIVER.—On the initiative of
3 the Secretary or at the request of an applicant,
4 the Secretary shall grant a full waiver, as ap-
5 propriate, of the requirement to submit assess-
6 ments for a drug or biological product under
7 this subsection if the applicant certifies and the
8 Secretary finds that—

9 “(i) necessary studies are impossible
10 or highly impracticable (because, for exam-
11 ple, the number of patients is so small or
12 the patients are geographically dispersed);

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

17 “(iii) the drug or biological product—

18 “(I) does not represent a mean-
19 ingful therapeutic benefit over existing
20 therapies for pediatric patients; and

21 “(II) is not likely to be used in a
22 substantial number of pediatric pa-
23 tients.

24 “(B) PARTIAL WAIVER.—On the initiative
25 of the Secretary or at the request of an appli-

1 cant, the Secretary shall grant a partial waiver,
2 as appropriate, of the requirement to submit as-
3 sements for a drug or biological product
4 under this subsection with respect to a specific
5 pediatric age group if the applicant certifies
6 and the Secretary finds that—

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

12 “(ii) there is evidence strongly sug-
13 gesting that the drug or biological product
14 would be ineffective or unsafe in that age
15 group;

16 “(iii) the drug or biological product—

17 “(I) does not represent a mean-
18 ingful therapeutic benefit over existing
19 therapies for pediatric patients in that
20 age group; and

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

24 “(iv) the applicant can demonstrate
25 that reasonable attempts to produce a pe-

1 diatric formulation necessary for that age
2 group have failed.

3 “(C) PEDIATRIC FORMULATION NOT POS-
4 SIBLE.—If a waiver is granted on the ground
5 that it is not possible to develop a pediatric for-
6 mulation, the waiver shall cover only the pedi-
7 atric groups requiring that formulation.

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

15 “(b) MARKETED DRUGS AND BIOLOGICAL PROD-
16 UCTS.—

17 “(1) IN GENERAL.—After providing notice in
18 the form of a letter and an opportunity for written
19 response and a meeting, which may include an advi-
20 sory committee meeting, the Secretary may (by
21 order in the form of a letter) require the holder of
22 an approved application for a drug under section
23 505 or the holder of a license for a biological prod-
24 uct under section 351 of the Public Health Service
25 Act (42 U.S.C. 262) to submit by a specified date

1 the assessments described in subsection (a)(2) if the
2 Secretary finds that—

3 “(A)(i) the drug or biological product is
4 used for a substantial number of pediatric pa-
5 tients for the labeled indications; and

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

8 “(B)(i) there is reason to believe that the
9 drug or biological product would represent a
10 meaningful therapeutic benefit over existing
11 therapies for pediatric patients for 1 or more of
12 the claimed indications; and

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

15 “(2) WAIVERS.—

16 “(A) FULL WAIVER.—At the request of an
17 applicant, the Secretary shall grant a full waiv-
18 er, as appropriate, of the requirement to submit
19 assessments under this subsection if the appli-
20 cant certifies and the Secretary finds that—

21 “(i) necessary studies are impossible
22 or highly impracticable (because, for exam-
23 ple, the number of patients in that age
24 group is so small or patients in that age
25 group are geographically dispersed); or

1 “(ii) there is evidence strongly sug-
2 gesting that the drug or biological product
3 would be ineffective or unsafe in all pedi-
4 atric age groups.

5 “(B) PARTIAL WAIVER.—At the request of
6 an applicant, the Secretary shall grant a partial
7 waiver, as appropriate, of the requirement to
8 submit assessments under this subsection with
9 respect to a specific pediatric age group if the
10 applicant certifies and the Secretary finds
11 that—

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

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

21 “(iii)(I) the drug or biological prod-
22 uct—

23 “(aa) does not represent a mean-
24 ingful therapeutic benefit over existing

1 therapies for pediatric patients in that
2 age group; and

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

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

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

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

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

1 “(3) RELATIONSHIP TO OTHER PEDIATRIC PRO-
2 VISIONS.—

3 “(A) NO ASSESSMENT WITHOUT WRITTEN
4 REQUEST.—No assessment may be required
5 under paragraph (1) for a drug subject to an
6 approved application under section 505 un-
7 less—

8 “(i) the Secretary has issued a written
9 request for a related pediatric study under
10 section 505A(e) of this Act or section 409I
11 of the Public Health Service Act (42
12 U.S.C. 284m);

13 “(ii)(I) if the request was made under
14 section 505A(e)—

15 “(aa) the recipient of the written
16 request does not agree to the request;
17 or

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

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

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 409I(c)(2) of that Act; and

7 “(iii)(I) the Secretary certifies under
8 subparagraph (B) that there are insuffi-
9 cient funds under sections 409I and 499 of
10 the Public Health Service Act (42 U.S.C.
11 284m, 290b) to conduct the study; or

12 “(II) the Secretary publishes in the
13 Federal Register a certification that cer-
14 tifies that—

15 “(aa) no contract or grant has
16 been awarded under section 409I or
17 499 of the Public Health Service Act
18 (42 U.S.C. 284m, 290b); and

19 “(bb) not less than 270 days
20 have passed since the date of a certifi-
21 cation under subparagraph (B) that
22 there are sufficient funds to conduct
23 the study.

24 “(B) NO AGREEMENT TO REQUEST.—Not
25 later than 60 days after determining that no

1 holder will agree to the written request (includ-
2 ing a determination that the Secretary has not
3 received a response specified under section
4 505A(d) of this Act or section 409I of the Pub-
5 lic Health Service Act (42 U.S.C. 284m), the
6 Secretary shall certify whether the Secretary
7 has sufficient funds to conduct the study under
8 section 409I or 499 of the Public Health Serv-
9 ice Act (42 U.S.C. 284m, 290b), taking into ac-
10 count the prioritization under section 409I.

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

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

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

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

6 “(1) the drug or biological product that is the
7 subject of the assessment or request may be consid-
8 ered misbranded and subject to relevant enforcement
9 action (except that the drug or biological product
10 shall not be subject to action under section 303); but

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

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

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

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

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

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

1 “(f) SCOPE OF AUTHORITY.—Nothing in this section
2 provides to the Secretary any authority to require a pedi-
3 atric assessment of any drug or biological product, or any
4 assessment regarding other populations or uses of a drug
5 or biological product, other than the pediatric assessments
6 described in this section.

7 “(g) ORPHAN DRUGS.—Unless the Secretary requires
8 otherwise by regulation, this section does not apply to any
9 drug for an indication for which orphan designation has
10 been granted under section 526.”.

11 (b) CONFORMING AMENDMENTS.—

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

15 (A) by striking “and (F)” and inserting
16 “(F)”; and

17 (B) by striking the period at the end and
18 inserting “, and (G) any assessments required
19 under section 505B.”.

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

22 (A) in the subsection heading, by striking
23 “REGULATIONS” and inserting “PEDIATRIC RE-
24 SEARCH REQUIREMENTS”; and

1 (B) by striking “pursuant to regulations
2 promulgated by the Secretary” and inserting
3 “by a provision of law (including a regulation)
4 other than this section”.

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

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

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

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

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

18 (a) ABBREVIATED NEW DRUG APPLICATION.—Sec-
19 tion 505A of the Federal Food, Drug, and Cosmetic Act
20 (21 U.S.C. 355a) is amended in subparagraphs (A) and
21 (B) of subsection (b)(2) and subparagraphs (A) and (B)
22 of subsection (c)(2) by striking “505(j)(4)(B)” and insert-
23 ing “505(j)(5)(B)”.

24 (b) PEDIATRIC ADVISORY COMMITTEE.—

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

5 (2) Section 14 of the Best Pharmaceuticals for
6 Children Act (42 U.S.C. 284m note; Public Law
7 107–109) is amended—

8 (A) in the section heading, by striking
9 **“PHARMACOLOGY”**;

10 (B) in subsection (a), by striking “(42
11 U.S.C. 217a),” and inserting (42 U.S.C. 217a)
12 or other appropriate authority,”;

13 (C) in subsection (b)—

14 (i) in paragraph (1), by striking “and
15 in consultation with the Director of the
16 National Institutes of Health”; and

17 (ii) in paragraph (2), by striking “and
18 505A” and inserting “505A, and 505B”;
19 and

20 (D) by striking “pharmacology” each place
21 it appears and inserting “therapeutics”.

22 (3) Section 15(a)(2)(A) of the Best Pharma-
23 ceuticals for Children Act (115 Stat. 1419) is
24 amended by striking “Pharmacology”.

1 (4) Section 16(1)(C) of the Best Pharma-
2 ceuticals for Children Act (21 U.S.C. 355a note;
3 Public Law 107–109) is amended by striking “Advi-
4 sory Subcommittee of the Anti-Infective Drugs”.

5 (5) Section 17(b)(1) of the Best Pharma-
6 ceuticals for Children Act (21 U.S.C. 355b(b)(1)) is
7 amended in the second sentence by striking “Advi-
8 sory Subcommittee of the Anti-Infective Drugs”.

9 (6) Paragraphs (8), (9), and (11) of section
10 409I(c) of the Public Health Service Act (42 U.S.C.
11 284m(c)) are amended by striking “Advisory Sub-
12 committee of the Anti-Infective Drugs” each place it
13 appears.

14 **SEC. 4. EFFECTIVE DATE.**

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

17 (b) NO LIMITATION OF AUTHORITY.—Neither the
18 lack of guidance or regulations to implement this Act or
19 the amendments made by this Act nor the pendency of
20 the process for issuing guidance or regulations shall limit
21 the authority of the Secretary of Health and Human Serv-
22 ices under, or defer any requirement under, this Act or
23 those amendments.

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