

108TH CONGRESS  
1ST SESSION

# S. 650

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## AN ACT

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”.

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

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

7 **“SEC. 505B. RESEARCH INTO PEDIATRIC USES FOR DRUGS**  
 8 **AND BIOLOGICAL PRODUCTS.**

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

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

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

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

21 shall submit with the application the assessments de-  
 22 scribed in paragraph (2).

23 “(2) ASSESSMENTS.—

24 “(A) IN GENERAL.—The assessments re-  
 25 ferred to in paragraph (1) shall contain data,  
 26 gathered using appropriate formulations for

1 each age group for which the assessment is re-  
2 quired, that are adequate—

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

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

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

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

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

1           age group can be extrapolated to another  
2           age group.

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

9           “(A) the Secretary finds that—

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

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

16           “(iii) there is another appropriate rea-  
17           son for deferral; and

18           “(B) the applicant submits to the  
19           Secretary—

20           “(i) certification of the grounds for  
21           deferring the assessments;

22           “(ii) a description of the planned or  
23           ongoing studies; and

24           “(iii) evidence that the studies are  
25           being conducted or will be conducted with

1 due diligence and at the earliest possible  
2 time.

3 “(4) WAIVERS.—

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

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

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

19 “(iii) the drug or biological product—

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

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

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

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

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

18           “(iii) the drug or biological product—

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

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

1                   “(iv) the applicant can demonstrate  
2                   that reasonable attempts to produce a pe-  
3                   diatric formulation necessary for that age  
4                   group have failed.

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

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

17                  “(b) MARKETED DRUGS AND BIOLOGICAL PROD-  
18                  UCTS.—

19                  “(1) IN GENERAL.—After providing notice in  
20                  the form of a letter and an opportunity for written  
21                  response and a meeting, which may include an advi-  
22                  sory committee meeting, the Secretary may (by  
23                  order in the form of a letter) require the holder of  
24                  an approved application for a drug under section  
25                  505 or the holder of a license for a biological prod-

1       uct under section 351 of the Public Health Service  
2       Act (42 U.S.C. 262) to submit by a specified date  
3       the assessments described in subsection (a)(2) if the  
4       Secretary finds that—

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

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

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

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

17       “(2) WAIVERS.—

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

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



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

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

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

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

23 “(iii)(I) the drug or biological  
24 product—

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

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

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

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

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

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

1 in the labeling for the drug or biological prod-  
2 uct.

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

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

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

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

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

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

23 “(II) if the request was made under  
24 section 409I of the Public Health Service  
25 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 solely because of that failure and  
9 subject to relevant enforcement action (except that  
10 the drug or biological product shall not be subject to  
11 action under section 303); but

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

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

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

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

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

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

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

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

13          “(h) INTEGRATION WITH OTHER PEDIATRIC STUD-  
14          IES.—The authority under this section shall remain in ef-  
15          fect so long as an application subject to this section may  
16          be accepted for filing by the Secretary on or before the  
17          date specified in section 505A(n).”.

18          (b) CONFORMING AMENDMENTS.—

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

22                         (A) by striking “and (F)” and inserting  
23                         “(F)”; and

1 (B) by striking the period at the end and  
2 inserting “, and (G) any assessments required  
3 under section 505B.”.

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

6 (A) in the subsection heading, by striking  
7 “REGULATIONS” and inserting “PEDIATRIC RE-  
8 SEARCH REQUIREMENTS”; and

9 (B) by striking “pursuant to regulations  
10 promulgated by the Secretary” and inserting  
11 “by a provision of law (including a regulation)  
12 other than this section”.

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

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

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

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



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

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

8 (b) PEDIATRIC ADVISORY COMMITTEE.—

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

13 (2) Section 14 of the Best Pharmaceuticals for  
14 Children Act (42 U.S.C. 284m note; Public Law  
15 107–109) is amended—

16 (A) in the section heading, by striking  
17 “**PHARMACOLOGY**”;

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

21 (C) in subsection (b)—

22 (i) in paragraph (1), by striking “and  
23 in consultation with the Director of the  
24 National Institutes of Health”; and

1 (ii) in paragraph (2), by striking “and  
2 505A” and inserting “505A, and 505B”;  
3 and

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

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

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

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

17 (6) Paragraphs (8), (9), and (11) of section  
18 409I(c) of the Public Health Service Act (42 U.S.C.  
19 284m(c)) are amended by striking “Advisory Sub-  
20 committee of the Anti-Infective Drugs” each place it  
21 appears.

22 **SEC. 4. EFFECTIVE DATE.**

23 (a) IN GENERAL.—Subject to subsection (b), this Act  
24 and the amendments made by this Act take effect on the  
25 date of enactment of this Act.

1 (b) APPLICABILITY TO NEW DRUGS AND BIOLOGICAL  
2 PRODUCTS.—

3 (1) IN GENERAL.—Subsection (a) of section  
4 505B of the Federal Food, Drug, and Cosmetic Act  
5 (as added by section 2) shall apply to an application  
6 described in paragraph (1) of that subsection sub-  
7 mitted to the Secretary of Health and Human Serv-  
8 ices on or after April 1, 1999.

9 (2) WAIVERS AND DEFERRALS.—

10 (A) WAIVER OR DEFERRAL GRANTED.—If,  
11 with respect to an application submitted to the  
12 Secretary of Health and Human Services be-  
13 tween April 1, 1999, and the date of enactment  
14 of this Act, a waiver or deferral of pediatric as-  
15 sessments was granted under regulations of the  
16 Secretary then in effect, the waiver or deferral  
17 shall be a waiver or deferral under subsection  
18 (a) of section 505B of the Federal Food, Drug,  
19 and Cosmetic Act, except that any date speci-  
20 fied in such a deferral shall be extended by the  
21 number of days that is equal to the number of  
22 days between October 17, 2002, and the date of  
23 enactment of this Act.

24 (B) WAIVER AND DEFERRAL NOT GRANT-  
25 ED.—If, with respect to an application sub-

1           mitted to the Secretary of Health and Human  
2           Services between April 1, 1999, and the date of  
3           enactment of this Act, neither a waiver nor de-  
4           ferral of pediatric assessments was granted  
5           under regulations of the Secretary then in ef-  
6           fect, the person that submitted the application  
7           shall be required to submit assessments under  
8           subsection (a)(2) of section 505B of the Fed-  
9           eral Food, Drug, and Cosmetic Act on the date  
10          that is the later of—

11                       (i) the date that is 1 year after the  
12                       date of enactment of this Act; or

13                       (ii) such date as the Secretary may  
14                       specify under subsection (a)(3) of that sec-  
15                       tion;

16          unless the Secretary grants a waiver under sub-  
17          section (a)(4) of that section.

18          (c) NO LIMITATION OF AUTHORITY.—Neither the  
19          lack of guidance or regulations to implement this Act or  
20          the amendments made by this Act nor the pendency of  
21          the process for issuing guidance or regulations shall limit  
22          the authority of the Secretary of Health and Human Serv-

1 ices under, or defer any requirement under, this Act or  
2 those amendments.

Passed the Senate July 23 (legislative day, July 21),  
2003.

Attest:

*Secretary.*

108TH CONGRESS  
1ST SESSION

**S. 650**

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**AN ACT**

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.