

[Committee Print]

110TH CONGRESS
1ST SESSION

H. R. _____

To amend the Federal Food, Drug, and Cosmetic Act with respect to pediatric research improvement, and for other purposes.

IN THE HOUSE OF REPRESENTATIVES

M____. _____ introduced the following bill; which was referred to the Committee on _____

A BILL

To amend the Federal Food, Drug, and Cosmetic Act with respect to pediatric research improvement, and for other purposes.

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. REAUTHORIZATION OF PEDIATRIC RESEARCH**
4 **EQUITY ACT.**

5 Section 505B of the Federal Food, Drug, and Cos-
6 metic Act (21 U.S.C. 355c) is amended to read as follows:

1 **“SEC. 505B. RESEARCH INTO PEDIATRIC USES FOR DRUGS**
2 **AND BIOLOGICAL PRODUCTS.**

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

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

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

10 “(B) under section 351 of the Public
11 Health Service Act (42 U.S.C. 262) for a new
12 active ingredient, new indication, new dosage
13 form, new dosing regimen, or new route of ad-
14 ministration; shall submit with the application
15 the assessments described in paragraph (2).

16 “(2) ASSESSMENTS.—

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

22 “(i) to assess the safety and effective-
23 ness of the drug or the biological product
24 for the claimed indications in all relevant
25 pediatric subpopulations; and

1 “(ii) to support dosing and adminis-
2 tration for each pediatric subpopulation for
3 which the drug or the biological product is
4 safe and effective.

5 “(B) SIMILAR COURSE OF DISEASE OR
6 SIMILAR EFFECT OF DRUG OR BIOLOGICAL
7 PRODUCT.—

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

17 “(ii) EXTRAPOLATION BETWEEN AGE
18 GROUPS.—A study may not be needed in
19 each pediatric age group if data from one
20 age group can be extrapolated to another
21 age group.

22 “(iii) INFORMATION ON EXTRAPO-
23 LATION.—A brief documentation of the sci-
24 entific data supporting the conclusion
25 under clauses (i) and (ii) shall be included

1 in the medical review that is collected as
2 part of the application under section 505
3 of this Act or section 351 of the Public
4 Health Service Act (42 U.S.C. 262).

5 “(3) DEFERRAL.—

6 “(A) IN GENERAL.—On the initiative of
7 the Secretary or at the request of the applicant,
8 the Secretary may defer submission of some or
9 all assessments required under paragraph (1)
10 until a specified date after approval of the drug
11 or issuance of the license for a biological prod-
12 uct if—

13 “(i) the Secretary finds that—

14 “(I) the drug or biological prod-
15 uct is ready for approval for use in
16 adults before pediatric studies are
17 complete;

18 “(II) pediatric studies should be
19 delayed until additional safety or ef-
20 fectiveness data have been collected;
21 or

22 “(III) there is another appro-
23 priate reason for deferral; and

24 “(ii) the applicant submits to the Sec-
25 retary—

1 “(I) certification of the grounds
2 for deferring the assessments;

3 “(II) a description of the planned
4 or ongoing studies;

5 “(III) evidence that the studies
6 are being conducted or will be con-
7 ducted with due diligence and at the
8 earliest possible time; and

9 “(IV) a timeline for the comple-
10 tion of such studies.

11 “(B) ANNUAL REVIEW.—

12 “(i) IN GENERAL.—On an annual
13 basis following the approval of a deferral
14 under subparagraph (A), the applicant
15 shall submit to the Secretary the following
16 information:

17 “(I) Information detailing the
18 progress made in conducting pediatric
19 studies.

20 “(II) If no progress has been
21 made in conducting such studies, evi-
22 dence and documentation that such
23 studies will be conducted with due
24 diligence and at the earliest possible
25 time.

1 “(ii) PUBLIC AVAILABILITY.—The in-
2 formation submitted through the annual
3 review under clause (I) shall promptly be
4 made available to the public in an easily
5 accessible manner, including through the
6 website of the Food and Drug Administra-
7 tion.

8 “(4) WAIVERS.—

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

16 “(i) necessary studies are impossible
17 or highly impracticable (because, for exam-
18 ple, the number of patients is so small or
19 the patients 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 all pedi-
23 atric age groups; or

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; 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. An ap-
17 plicant seeking either a full or partial waiver
18 shall submit to the Secretary documentation de-
19 tailing why a pediatric formulation cannot be
20 developed and, if the waiver is granted, the ap-
21 plicant’s submission shall promptly be made
22 available to the public in an easily accessible
23 manner, including through posting on the
24 website of the Food and Drug Administration.

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

8 “(b) MARKETED DRUGS AND BIOLOGICAL PROD-
9 UCTS.—

10 “(1) IN GENERAL.—After providing notice in
11 the form of a letter and an opportunity for written
12 response and a meeting, which may include an advi-
13 sory committee meeting, the Secretary may (by
14 order in the form of a letter) require the sponsor or
15 holder of an approved application for a drug under
16 section 505 or the holder of a license for a biological
17 product under section 351 of the Public Health
18 Service Act (42 U.S.C. 262) to submit by a specified
19 date the assessments described in subsection (a)(2)
20 and the written request, as appropriate, if the Sec-
21 retary finds that—

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

1 “(ii) adequate pediatric labeling could con-
2 fer a benefit on pediatric patients;

3 “(B) there is reason to believe that the
4 drug or biological product would represent a
5 meaningful therapeutic benefit over existing
6 therapies for pediatric patients for 1 or more of
7 the claimed indications; or

8 “(C) the absence of adequate pediatric la-
9 beling could pose a risk to pediatric patients.

10 “(2) WAIVERS.—

11 “(A) FULL WAIVER.—At the request of an
12 applicant, the Secretary shall grant a full waiv-
13 er, as appropriate, of the requirement to submit
14 assessments under this subsection if the appli-
15 cant certifies and the Secretary finds that—

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

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

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

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

17 “(iii)(I) the drug or biological prod-
18 uct—

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

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

1 “(II) the absence of adequate labeling
2 could not pose significant risks to pediatric
3 patients; or

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

8 “(C) PEDIATRIC FORMULATION NOT POS-
9 SIBLE.—If a waiver is granted on the ground
10 that it is not possible to develop a pediatric for-
11 mulation, the waiver shall cover only the pedi-
12 atric groups requiring that formulation. An ap-
13 plicant seeking either a full or partial waiver
14 shall submit to the Secretary documentation de-
15 tailing why a pediatric formulation cannot be
16 developed and, if the waiver is granted, the ap-
17 plicant’s submission shall promptly be made
18 available to the public in an easily accessible
19 manner, including through posting on the
20 website of the Food and Drug Administration.

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

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

3 “(c) MEANINGFUL THERAPEUTIC BENEFIT.—For
4 the purposes of paragraph (4)(A)(iii)(I) and (4)(B)(iii)(I)
5 of subsection (a) and paragraphs (1)(B)(I) and
6 (2)(B)(iii)(I)(aa) of subsection (b), a drug or biological
7 product shall be considered to represent a meaningful
8 therapeutic benefit over existing therapies if the Secretary
9 determines that—

10 “(1) if approved, the drug or biological product
11 could represent an improvement in the treatment,
12 diagnosis, or prevention of a disease, compared with
13 marketed products adequately labeled for that use in
14 the relevant pediatric population; or

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

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

23 “(1) the drug or biological product that is the
24 subject of the assessment or request may be consid-
25 ered misbranded solely because of that failure and

1 subject to relevant enforcement action (except that
2 the drug or biological product shall not be subject to
3 action under section 303); but

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

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

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

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

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

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

19 “(f) REVIEW OF PEDIATRIC ASSESSMENTS, DEFER-
20 RALS, AND WAIVERS.—

21 “(1) REVIEW.—The Secretary shall create an
22 internal committee to review all pediatric assess-
23 ments issued under this section and all deferral and
24 waiver requests made pursuant to this section. Such
25 internal committee shall include individuals, each of

1 whom is an employee of the Food and Drug Admin-
2 istration, with expertise in pediatrics, biopharma-
3 cology, statistics, drugs and drug formulations, legal
4 issues, pediatric ethics, the appropriate expertise,
5 such as expertise in child and adolescent psychiatry,
6 pertaining to the pediatric product under review, one
7 or more experts from the Office of Pediatric Thera-
8 peutics, and other individuals designated by the Sec-
9 retary.

10 “(2) ACTION BY COMMITTEE.—The committee
11 established under paragraph (1) may perform a
12 function under this section using appropriate mem-
13 bers of the committee described in paragraph (1)
14 and need not convene all members of the committee
15 described in paragraph (1) in order to perform a
16 function under this section.

17 “(3) DOCUMENTATION OF COMMITTEE AC-
18 TION.—For each drug or biological product, the
19 committee established under this paragraph shall
20 document for each function described in paragraph
21 (4) which members of the committee participated in
22 such function.

23 “(4) REVIEW OF REQUESTS FOR PEDIATRIC AS-
24 SESSMENTS, DEFERRALS AND WAIVERS.—All re-
25 quests for a pediatric assessment issued pursuant to

1 this section and all requests for deferrals and waiv-
2 ers from the requirement to conduct a pediatric as-
3 sessment under this section shall be reviewed by the
4 committee established under paragraph (1).

5 “(5) TRACKING OF ASSESSMENTS AND LABEL-
6 ING CHANGES.—The Secretary shall track and make
7 available to the public in an easily accessible man-
8 ner, including through post on the website of the
9 Food and Drug Administration—

10 “(A) the number of assessments conducted
11 under this section;

12 “(B) the specific drugs and biological prod-
13 ucts and their uses assessed under this section;

14 “(C) the types of assessments conducted
15 under this section, including trial design, the
16 number of pediatric patients studied, and the
17 number of centers and countries involved;

18 “(D) the total number of deferrals re-
19 quested and granted under this section and, if
20 granted, the reasons for such deferrals, the
21 timeline for completion, and the number com-
22 pleted and pending by the specified date, as
23 outlined in subsection (a)(3);

1 “(E) the number of waivers requested and
2 granted under this section and, if granted, the
3 reasons for the waivers;

4 “(F) the number of pediatric formulations
5 developed and the number of pediatric formula-
6 tions not developed and the reasons any such
7 formulation were not developed;

8 “(G) the labeling changes made as a result
9 of assessments conducted under this section;

10 “(H) an annual summary of labeling
11 changes made as a result of assessments con-
12 ducted under this section for distribution pursu-
13 ant to subsection (h)(2); and

14 “(I) an annual summary of information
15 submitted pursuant to subsection (a)(3)(B).

16 “(6) COMMITTEE.—The committee established
17 under paragraph (1) is the committee established
18 under section 505A(f)(1).

19 “(g) LABELING CHANGES.—

20 “(1) PRIORITY STATUS FOR PEDIATRIC APPLI-
21 CATIONS.—Any supplement to an application under
22 section 505 and section 351 of the Public Health
23 Service Act proposing a labeling change as a result
24 of any pediatric assessments conducted pursuant to
25 this section—

1 “(A) shall be considered a priority applica-
2 tion or supplement; and

3 “(B) shall be subject to the performance
4 goals established by the Commissioner for pri-
5 ority drugs.

6 “(2) DISPUTE RESOLUTION.—

7 “(A) REQUEST FOR LABELING CHANGE
8 AND FAILURE TO AGREE.—If the Commissioner
9 determines that a sponsor and the Commis-
10 sioner have been unable to reach agreement on
11 appropriate changes to the labeling for the drug
12 that is the subject of the application or supple-
13 ment, not later than 180 days after the date of
14 the submission of the application or supple-
15 ment—

16 “(i) the Commissioner shall request
17 that the sponsor of the application make
18 any labeling change that the Commissioner
19 determines to be appropriate; and

20 “(ii) if the sponsor does not agree
21 within 30 days after the Commissioner’s
22 request to make a labeling change re-
23 quested by the Commissioner, the Commis-
24 sioner shall refer the matter to the Pedi-
25 atric Advisory Committee.

1 “(B) ACTION BY THE PEDIATRIC ADVISORY
2 COMMITTEE.—Not later than 90 days after re-
3 ceiving a referral under subparagraph (A)(ii),
4 the Pediatric Advisory Committee shall—

5 “(i) review the pediatric study reports;
6 and

7 “(ii) make a recommendation to the
8 Commissioner concerning appropriate la-
9 beling changes, if any.

10 “(C) CONSIDERATION OF RECOMMENDA-
11 TIONS.—The Commissioner shall consider the
12 recommendations of the Pediatric Advisory
13 Committee and, if appropriate, not later than
14 30 days after receiving the recommendation,
15 make a request to the sponsor of the applica-
16 tion to make any labeling changes that the
17 Commissioner determines to be appropriate.

18 “(D) MISBRANDING.—If the sponsor of the
19 application, within 30 days after receiving a re-
20 quest under subparagraph (c), does not agree to
21 make a labeling change requested by the Com-
22 missioner, the Commissioner may deem the
23 drug that is the subject of the application to be
24 misbranded.

1 “(E) NO EFFECT ON AUTHORITY.—Noth-
2 ing in this subsection limits the authority of the
3 United States to bring an enforcement action
4 under this Act when a drug lacks appropriate
5 pediatric labeling. Neither course of action (the
6 Pediatric Advisory Committee process or an en-
7 forcement action referred to in the preceding
8 sentence) shall preclude, delay, or serve as the
9 basis to stay the other course of action.

10 “(3) OTHER LABELING CHANGES.—If the Sec-
11 retary makes a determination that a pediatric as-
12 sessment conducted under this section does or does
13 not demonstrate that the drug that is the subject of
14 such assessment is safe and effective in pediatric
15 populations or subpopulations, including whether
16 such assessment results are inconclusive, the Sec-
17 retary shall order the label of such product to in-
18 clude information about the results of the assess-
19 ment and a statement of the Secretary’s determina-
20 tion.

21 “(h) DISSEMINATION OF PEDIATRIC INFORMA-
22 TION.—

23 “(1) IN GENERAL.—Not later than 180 days
24 after the date of submission of a pediatric assess-
25 ment under this section, the Secretary shall make

1 available to the public in an easily accessible manner
2 the medical, statistical, and clinical pharmacology re-
3 views of such pediatric assessments, and shall post
4 such assessments on the website of the Food and
5 Drug Administration.

6 “(2) DISSEMINATION OF INFORMATION RE-
7 GARDING LABELING CHANGES.—The Secretary shall
8 require that the sponsors of the assessments that re-
9 sult in labeling changes that are reflected in the an-
10 nual summary developed pursuant to subsection
11 (f)(5)(H) distribute such information to physicians
12 and other health care providers.

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

17 “(i) ADVERSE EVENT REPORTING.—

18 “(1) REPORTING IN YEAR ONE.—During the
19 one-year period beginning on the date a labeling
20 change is made pursuant to subsection (g), the Sec-
21 retary shall ensure that all adverse event reports
22 that have been received for such drug (regardless of
23 when such report was received) are referred to the
24 Office of Pediatric Therapeutics. In considering the
25 report, the Director of such Office shall provide for

1 the review of the report by the Pediatric Advisory
2 Committee, including obtaining any recommenda-
3 tions of such committee regarding whether the Sec-
4 retary should take action under this Act in response
5 to such report.

6 “(2) REPORTING IN SUBSEQUENT YEARS.—Fol-
7 lowing the one-year period described in paragraph
8 (1), the Secretary shall, as appropriate, refer to the
9 Office of Pediatric Therapeutics all pediatric adverse
10 event reports for a drug for which a pediatric study
11 was conducted under this section. In considering the
12 report, the Director of such Office may provide for
13 the review of the report by the Pediatric Advisory
14 Committee, including obtaining any recommendation
15 of such Committee regarding whether the Secretary
16 should take action in response to such report.

17 “(3) EFFECT.—The requirements of this sub-
18 section shall supplement, not supplant, other review
19 of such adverse event reports by the Secretary.

20 “(j) SCOPE OF AUTHORITY.—Nothing in this section
21 provides to the Secretary any authority to require a pedi-
22 atric assessment of any drug or biological product, or any
23 assessment regarding other populations or uses of a drug
24 or biological product, other than the pediatric assessments
25 described in this section.

1 “(k) ORPHAN DRUGS.—Unless the Secretary re-
2 quires otherwise by regulation, this section does not apply
3 to any drug for an indication for which orphan designation
4 has been granted under section 526.

5 “(l) INSTITUTE OF MEDICINE STUDY.—

6 “(1) IN GENERAL.—Not later than three years
7 after the date of the enactment of the Improving
8 Pharmaceuticals for Children Act of 2007, the Sec-
9 retary shall contract with the Institute of Medicine
10 to conduct a study and report to Congress regarding
11 the pediatric studies conducted pursuant to this sec-
12 tion since 1997.

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

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

18 “(B) the use of extrapolation for pediatric
19 subpopulations, the use of alternative endpoints
20 for pediatric populations, neonatal assessment
21 tools, the number and type of pediatric adverse
22 events, and ethical issues in pediatric clinical
23 trials.

24 “(3) REPRESENTATIVE SAMPLE.—The Institute
25 of Medicine may devise an appropriate mechanism to

1 review a representative sample of studies conducted
2 pursuant to this section from each review division
3 within the Center for Drug Evaluation and Research
4 in order to make the requested assessment.”.