112TH CONGRESS
2D SESSION

S. 2289

To amend the Federal Food, Drug, and Cosmetic Act with respect to pediatric provisions.

IN THE SENATE OF THE UNITED STATES

APRIL 17, 2012

Mr. REED (for himself, Mr. ALEXANDER, Mrs. MURRAY, and Mr. ROBERTS) introduced the following bill; which was read twice and referred to the Committee on Health, Education, Labor, and Pensions

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A BILL

To amend the Federal Food, Drug, and Cosmetic Act with respect to pediatric provisions.

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 ''Better Pharmaceuticals and Devices for Children Act of 2012''.

SEC. 2. TABLE OF CONTENTS; REFERENCES IN ACT.

(a) TABLE OF CONTENTS.—The table of contents for this Act is as follows:

(b) REFERENCES IN ACT.—Except as otherwise specified, amendments made by this Act to a section or other provision of law are amendments to such section or other provision of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 301 et seq.).

SEC. 3. PERMANENCE.

(a) PEDIATRIC STUDIES OF DRUGS.—Subsection (q) of section 505A (21 U.S.C. 355a) is amended—

(1) in paragraph (1), by striking ''on or before October 1, 2012,''; and

(2) in paragraph (2), by striking ''on or before October 1, 2012,''.

(b) RESEARCH INTO PEDIATRIC USES FOR DRUGS AND BIOLOGICAL PRODUCTS.—Section 505B (21 U.S.C. 355c) is amended—

(1) by striking subsection (m); and

(2) by redesignating subsection (n) as subsection (m).

SEC. 4. WRITTEN REQUESTS.

(a) FEDERAL FOOD, DRUG, AND COSMETIC ACT.—Subsection (h) of section 505A (21 U.S.C. 355a) is amended to read as follows:

''(h) RELATIONSHIP TO PEDIATRIC RESEARCH REQUIREMENTS.—Exclusivity under this section shall only be granted for the completion of a study or studies that are the subject of a written request and for which reports are submitted and accepted in accordance with subsection (d)(3). Written requests under this section may consist of a study or studies required under section 505B.''.

(b) PUBLIC HEALTH SERVICE ACT.—Section 351(m) of the Public Health Service Act (42 U.S.C. 262(m)) is amended by striking ''(f), (i), (j), (k), (l), (p), and (q)'' and inserting ''(f), (h), (i), (j), (k), (l), and (p)''.

SEC. 5. COMMUNICATION WITH PEDIATRIC REVIEW COMMITTEE.

Not later than 1 year after the date of enactment of this Act, the Secretary of Health and Human Services (referred to in this Act as the ''Secretary'') shall issue internal standard operating procedures that provide for the review by the internal review committee established under section 505C of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355d) of any significant modifications to initial pediatric study plans, agreed pediatric study plans, and written requests under sections 505A and 505B of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355c). Such internal standard operating procedures shall

be made publicly available on the Internet Web site of the Food and Drug Administration.

SEC. 6. ACCESS TO DATA.

Not later than 3 years after the date of enactment of this Act, the Secretary shall make available to the public, including through posting on the Internet Web site of the Food and Drug Administration, the medical, statistical, and clinical pharmacology reviews of, and corresponding written requests issued to an applicant, sponsor, or holder for, pediatric studies submitted between January 4, 2002, and September 27, 2007, under subsection (b) or (c) of section 505A of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355a) for which 6 months of market exclusivity was granted and that resulted in a labeling change. The Secretary shall make public the information described in the preceding sentence in a manner consistent with how the Secretary releases information under section 505A(k) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355a(k)).

SEC. 7. ENSURING THE COMPLETION OF PEDIATRIC STUDIES.

(a) EXTENSION OF DEADLINE FOR DEFERRED STUDIES.—Section 505B (21 U.S.C. 355c) is amended—

(1) in subsection (a)(3)—

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

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

''(B) DEFERRAL EXTENSION.—

''(i) IN GENERAL.—On the initiative of the Secretary or at the request of the applicant, the Secretary may grant an extension of a deferral approved under subparagraph (A) for submission of some or all assessments required under paragraph (1) if—

''(I) the Secretary determines that the conditions described in subclause (II) or (III) of subparagraph (A)(i) continue to be met; and

''(II) the applicant submits a new timeline under subparagraph (A)(ii)(IV) and any significant updates to the information required under subparagraph (A)(ii).

''(ii) TIMING AND INFORMATION.—If the deferral extension under this subparagraph is requested by the applicant, the applicant shall submit the deferral exten-

sion request containing the information described in this subparagraph not less than 90 days prior to the date that the deferral would expire but for the requested extension. The Secretary shall respond to such request not later than 45 days after the receipt of such letter. If the Secretary grants such an extension, the specified date shall be considered the extended date. The sponsor of the required assessment under paragraph (1) shall not be issued a letter described in subsection (d) unless the specified date of submission for such required studies has passed or if the request for an extension is pending. For a deferral that has expired prior to the date of enactment of the Better Pharmaceuticals and Devices for Children Act of 2012 or that will expire prior to 270 days after the date of enactment of such Act, a deferral extension shall be requested by an applicant not later than 180 days after the date of enactment of such Act. Nothing in this clause shall prevent the Secretary from updating the status of a study or studies publicly if

components of such study or studies are late or delayed.''; and

(C) in subparagraph (C), as so redesignated—

(i) in clause (i), by adding at the end the following:

''(III) Projected completion date for pediatric studies.

''(IV) The reason or reasons why a deferral or deferral extension continues to be necessary.''; and

(ii) in clause (ii)—

(I) by inserting '', as well as the date of each deferral or deferral extension, as applicable,'' after ''clause (i)''; and

(II) by inserting ''not later than 60 days after submission to the Secretary'' after ''Administration''; and

(2) in subsection (f)—

(A) in the subsection heading, by inserting ''DEFERRAL EXTENSIONS,'' after ''DEFERRALS,'';

(B) in paragraph (1), by inserting '', deferral extension,'' after ''deferral''; and

(C) in paragraph (4), by inserting ", deferral extensions," after "deferrals".

(b) TRACKING OF EXTENSIONS; ANNUAL INFORMATION.—Section 505B(f)(6)(D) (21 U.S.C. 355c(f)(6)(D)) is amended to read as follows:

"(D) aggregated on an annual basis—

"(i) the total number of deferrals and deferral extensions requested and granted under this section and, if granted, the reasons for each such deferral or deferral extension;

"(ii) the timeline for completion of the assessments; and

"(iii) the number of assessments completed and pending by the specified date, as outlined in subsection (a)(3);".

(c) ACTION ON FAILURE TO COMPLETE STUDIES.—

(1) ISSUANCE OF LETTER.—Subsection (d) of section 505B (21 U.S.C. 355c) is amended to read as follows:

"(d) SUBMISSION OF ASSESSMENTS.—If a person fails to submit a required assessment described in subsection (a)(2), fails to meet the applicable requirements in subsection (a)(3), or fails to submit a request for approval of a pediatric formulation described in subsection

(a) or (b), in accordance with applicable provisions of subsections (a) and (b), the following shall apply:

''(1) Beginning 270 days after the date of enactment of the Better Pharmaceuticals and Devices for Children Act of 2012, the Secretary shall issue a letter to such person informing them of such failure to submit or meet the applicable subsection. Such letter shall require the person to respond in writing within 45 calendar days of issuance of such letter. Such response may include the person's request for a deferral extension if applicable. Such letter and the person's written response to such letter shall be made publicly available on the Internet Web site of the Food and Drug Administration 45 calendar days after issuance, with redactions for any trade secrets and confidential commercial information. If the Secretary determines that the letter was issued in error, the requirements of this paragraph shall not apply.

''(2) The drug or biological product that is the subject of an assessment described in subsection (a)(2), applicable requirements in subsection (a)(3), or request for approval of a pediatric formulation, may be considered misbranded solely because of that failure and subject to relevant enforcement action

(except that the drug or biological product shall not be subject to action under section 303), but such failure 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.".

(2) TRACKING OF LETTERS ISSUED.—Subparagraph (D) of section 505B(f)(6) (21 U.S.C. 355c(f)(6)), as amended by subsection (b), is further amended—

(A) in clause (ii), by striking "; and" and inserting a semicolon;

(B) in clause (iii), by adding "and" at the end; and

(C) by adding at the end the following:

"(iv) the number of postmarket noncompliance letters issued pursuant to subsection (d), and the recipients of such letters;".

SEC. 8. PEDIATRIC STUDY PLANS.

(a) IN GENERAL.—Subsection (e) of section 505B (21 U.S.C. 355c) is amended to read as follows:

"(e) PEDIATRIC STUDY PLANS.—

''(1) IN GENERAL.—An applicant subject to subsection (a) shall submit to the Secretary an initial pediatric study plan prior to the submission of the assessments described under subsection (a)(2).

''(2) TIMING; CONTENT; MEETING.—

''(A) TIMING.—An applicant shall submit an initial pediatric study plan to the Secretary not later than 60 calendar days after the date of the end of phase II meeting or such other equivalent time agreed upon between the Secretary and the applicant. Nothing in this paragraph shall preclude the Secretary from accepting the submission of an initial pediatric study plan earlier than the date described under the preceding sentence.

''(B) CONTENT OF INITIAL PLAN.—The initial pediatric study plan shall include—

''(i) an outline of the pediatric study or studies that the applicant plans to conduct (including, to the extent practicable study objectives and design, age groups, relevant endpoints, and statistical approach);

''(ii) any request for a deferral, partial waiver, or waiver under this section, if ap-

plicable, along with any supporting information; and

''(iii) other information specified in the regulations promulgated under paragraph (4).

''(C) MEETING.—The Secretary—

''(i) shall meet with the applicant to discuss the initial pediatric study plan not later than 60 calendar days after the receipt of such plan under subparagraph (A);

''(ii) may determine that a written response to the initial pediatric study plan is sufficient to communicate comments on the initial pediatric study plan, and that no meeting is necessary; and

''(iii) if the Secretary determines that no meeting is necessary, shall so notify the applicant and provide written comments of the Secretary not later than 60 calendar days after the receipt of the initial pediatric study plan.

''(3) AGREED PEDIATRIC STUDY PLAN.—The applicant shall document agreement on the initial pediatric study plan in a submission to the Secretary marked 'Agreed Pediatric Study Plan', and the Sec-

retary shall confirm such agreement to the applicant in writing not later than 30 calendar days of receipt of such agreed pediatric study plan.

''(4) DEFERRAL AND WAIVER.—If the agreed pediatric study plan contains a request from the applicant for a deferral, partial waiver, or waiver under this section, the written confirmation under paragraph (3) shall include a recommendation from the Secretary as to whether such request meets the standards under paragraphs (3) or (4) of subsection (a).

''(5) AMENDMENTS TO THE PLAN.—At the initiative of the Secretary or the applicant, the agreed pediatric study plan may be amended at any time. The requirements of paragraph (2)(C) shall apply to any such proposed amendment in the same manner and to the same extent as such requirements apply to an initial pediatric study plan under paragraph (1). The requirements of paragraphs (3) and (4) shall apply to any agreement resulting from such proposed amendment in the same manner and to the same extent as such requirements apply to an agreed pediatric study plan.

''(6) INTERNAL COMMITTEE.—The Secretary shall consult the internal committee under section

505C on the review of the initial pediatric plan, agreed pediatric plan, and any amendments to such plans.

''(7) REQUIRED RULEMAKING.—Not later than 1 year after the date of enactment of the Better Pharmaceuticals and Devices for Children Act of 2012, the Secretary shall promulgate proposed regulations and issue proposed guidance to implement the provisions of this subsection.''.

(b) CONFORMING AMENDMENTS.—Section 505B (21 U.S.C. 355c) is amended—

(1) by amending subclause (II) of subsection (a)(3)(A)(ii) to read as follows:

''(II) a pediatric study plan as described in subsection (e);''; and

(2) in subsection (f)—

(A) in the subsection heading, by striking ''PEDIATRIC PLANS,'' and inserting ''PEDIATRIC STUDY PLANS,'';

(B) in paragraph (1), by striking ''all pediatric plans'' and inserting ''initial pediatric study plans, agreed pediatric study plans,''; and

(C) in paragraph (4)—

(i) in the paragraph heading, by striking ''PEDIATRIC PLANS,'' and inserting ''PEDIATRIC STUDY PLANS,''; and

(ii) by striking ''pediatric plans'' and inserting ''initial pediatric study plans, agreed pediatric study plans,''.

(c) EFFECTIVE DATES.—

(1) PEDIATRIC STUDY PLANS.—Subsection (e) of section 505B of the Federal Food, Drug, and Cosmetic Act (other than paragraph (4) of such subsection), as amended by subsection (a), shall take effect 180 days after the date of enactment of this Act, without regard to whether the Secretary has promulgated final regulations under paragraph (4) of such subsection by such date.

(2) CONFORMING AMENDMENTS.—The amendments made by subsection (b) shall take effect 180 days after the date of enactment of this Act.

SEC. 9. REAUTHORIZATIONS.

(a) PEDIATRIC ADVISORY COMMITTEE.—Section 14(d) of the Best Pharmaceuticals for Children Act (42 U.S.C. 284m note) is amended by striking ''Notwithstanding section 14 of the Federal Advisory Committee Act, the advisory committee shall continue to operate during the five-year period beginning on the date of the enact-

ment of the Best Pharmaceuticals for Children Act of 2007'' and inserting ''Section 14 of the Federal Advisory Committee Act shall not apply to the advisory committee''.

(b) PEDIATRIC SUBCOMMITTEE OF THE ONCOLOGIC DRUGS ADVISORY COMMITTEE.—Section 15(a)(3) of the Best Pharmaceuticals for Children Act (42 U.S.C. 284m note) is amended by striking '' during the five-year period beginning on the date of the enactment of the Best Pharmaceuticals for Children Act of 2007'' and inserting ''for the duration of the operation of the Oncologic Drugs Advisory Committee''.

(c) HUMANITARIAN DEVICE EXEMPTION EXTENSION.—Section 520(m)(6)(A)(iv) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360j(m)(6)(A)(iv)) is amended by striking ''2012'' and inserting ''2017''.

(d) DEMONSTRATION GRANTS TO IMPROVE PEDIATRIC DEVICE AVAILABILITY.—Section 305(e) of Pediatric Medical Device Safety and Improvement Act (Public Law 110–85; 42 U.S.C. 282 note) is amended by striking ''$6,000,000 for each of fiscal years 2008 through 2012'' and inserting ''$4,500,000 for each of fiscal years 2013 through 2017''.

(e) PROGRAM FOR PEDIATRIC STUDY OF DRUGS IN PHSA.—Section 409I(e)(1)(B) of the Public Health Service Act (42 U.S.C. 284m(e)(1)(B)) is amended by striking

''of the four succeeding fiscal years'' and inserting ''succeeding fiscal year''.

SEC. 10. REPORT.

(a) IN GENERAL.—Not later than January 1, 2016, and at the end of each subsequent 5-year period, the Comptroller General of the United States, in consultation with the Secretary of Health and Human Services, shall submit to Congress a report that evaluates the effectiveness of sections 505A and 505B of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355a, 355c) and section 409I of the Public Health Service Act (42 U.S.C. 284m) in ensuring that medicines used by children are tested in pediatric populations and properly labeled for use in children.

(b) CONTENTS.—The report under subsection (a) shall include—

(1) the number and importance of drugs and biological products for children that are being tested (as of the date of such report) under 505A and 505B of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355a, 355c) and section 409I of the Public Health Service Act (42 U.S.C. 284m), including—

(A) the number of labeling changes made to drugs and biological products pursuant to

such sections since the date of enactment of this Act; and

(B) the importance of such drugs and biological products in the improvement of the health of children;

(2) the number of requirements under such sections 505A and 505B that have not met by the initial deadline provided under such sections, including—

(A) the number of deferrals and deferral extensions granted and the reasons such extensions were granted;

(B) the number of waivers and partial waivers granted; and

(C) the number of letters issued under subsection (d) of such section 505B;

(3) the number of written requests issued and declined under such section 505A since the date of enactment of this Act (including the reasons for such declination), and a description and status of referrals made under subsection (n) of such section 505A;

(4) the number and importance of drugs and biological products for children that are not being tested for use in pediatric populations, notwith-

standing the existence of the programs under such sections 505A and 505B and section 409I of the Public Health Service Act;

(5) the possible reasons for the lack of testing reported under paragraph (4);

(6) the number of drugs and biological products for which testing is being done (as of the date of the report) and for which a labeling change is required under the programs described in paragraph (4), including—

(A) the date labeling changes are made;

(B) which labeling changes required the use of the dispute resolution process; and

(C) for labeling changes that required such dispute resolution process, a description of—

(i) the disputes;

(ii) the recommendations of the Pediatric Advisory Committee; and

(iii) the outcomes of such process; and

(D) an assessment of the effectiveness in improving information about pediatric uses of drugs and biological products;

(7)(A) the efforts made by the Secretary to increase the number of studies conducted in the neonatal population (including efforts made to encour-

age the conduct of appropriate studies in neonates by companies with products that have sufficient safety and other information to make the conduct of the studies ethical and safe); and

(B) the results of such efforts;

(8)(A) the number and importance of drugs and biological products for children with cancer that are being tested as a result of the programs described in paragraph (4); and

(B) any recommendations for modifications to such programs that would lead to new and better therapies for children with cancer, including a detailed rationale for each recommendation;

(9) an assessment of progress made in addressing the recommendations and findings of any prior report issued by the Comptroller General regarding the topics addressed in the report under this section, including with respect to—

(A) improving public access to information from pediatric studies conducted under such sections 505A and 505B; and

(B) improving the timeliness of pediatric studies and pediatric study planning under such sections 505A and 505B;

(10) any recommendations for modification to the programs that would improve pediatric drug research and increase pediatric labeling of drugs and biological products; and

(11) an assessment of the successes of and limitations to studying drugs for rare diseases under such sections 505A and 505B.

SEC. 11. TECHNICAL AMENDMENTS.

(a) PEDIATRIC STUDIES OF DRUGS IN FFDCA.—Section 505A (21 U.S.C. 355a) is amended—

(1) in subsection (k)(2), by striking ''subsection (f)(3)(F)'' and inserting ''subsection (f)(6)(F)'';

(2) in subsection (n)—

(A) in the subsection heading, by striking ''COMPLETED'' and inserting ''SUBMITTED''; and

(B) in paragraph (1)—

(i) in the matter preceding subparagraph (A), by striking ''have not been completed'' and inserting ''have not been submitted by the date specified in the written request issued'';

(ii) in subparagraph (A)—

(I) in the first sentence, by inserting '', or for which a period of ex-

clusivity eligible for extension under subsection (b)(1) or (c)(1) of this section or under subsection (m)(2) or (m)(3) of section 351 of the Public Health Service Act has not ended'' after ''expired''; and

(II) by striking ''Prior to'' and all that follows through the period at the end; and

(iii) in subparagraph (B), by striking ''no listed patents or has 1 or more listed patents that have expired,'' and inserting ''no unexpired listed patents and for which no unexpired periods of exclusivity eligible for extension under subsection (b)(1) or (c)(1) of this section or under subsection (m)(2) or (m)(3) of section 351 of the Public Health Service Act apply''; and

(3) in subsection (o)(2), by amendment subparagraph (B) to read as follows:

''(B) a statement of any appropriate pediatric contraindications, warnings, precautions, or other information that the Secretary considers necessary to assure safe use.''.

(b) RESEARCH INTO PEDIATRIC USES FOR DRUGS AND BIOLOGICAL PROJECTS IN FFDCA.—Section 505B (21 U.S.C. 355c) is amended—

(1) in subsection (a)—

(A) in paragraph (1)—

(i) in the matter preceding subparagraph (A), by inserting ''for a drug'' after ''(or supplement to an application)'';

(ii) in subparagraph (A), by striking ''for a'' and inserting '', including, with respect to a drug, an application (or supplement to an application) for a'';

(iii) in subparagraph (B), by striking ''for a'' and inserting '', including, with respect to a drug, an application (or supplement to an application) for a''; and

(iv) in the matter following subparagraph (B), by inserting ''(or supplement)'' after ''application''; and

(B) in paragraph (4)(C)—

(i) in the first sentence, by inserting ''partial'' before ''waiver is granted''; and

(ii) in the second sentence, by inserting ''such a'' after ''full or'';

(2) in subsection (b)(1), in the matter preceding subparagraph (A), by striking ''After providing notice'' and all that follows through ''studies), the'' and inserting ''The'';

(3) in subsection (g)—

(A) in paragraph (1)(A), by inserting ''that receives a priority review or 330 days after the date of the submission of an application or supplement that receives a standard review'' after ''after the date of the submission of the application or supplement''; and

(B) in paragraph (2), by striking ''the label of such product'' and inserting ''the labeling of such product''; and

(4) in subsection (h)(1)—

(A) by inserting ''an application (or supplement to an application) that contains'' after ''date of submission of''; and

(B) by inserting '', if the application (or supplement) receives a priority review, or not later than 330 days after the date of submission of an application (or supplement to an application) that contains a pediatric assessment under this section, if the application (or supple-

ment) receives a standard review,'' after ''under this section,''.

(c) INTERNAL REVIEW COMMITTEE.—The heading of section 505C (21 U.S.C. 355d) is amended by inserting ''**AND DEFERRAL EXTENSIONS**'' after ''**DEFERRALS**''.

(d) PROGRAM FOR PEDIATRIC STUDIES OF DRUGS.—Section 409I(c) of the Public Health Service Act (42 U.S.C. 284m(c)) is amended—

(1) in paragraph (1)—

(A) in the matter preceding subparagraph (A), by inserting ''or section 351(m) of this Act,'' after ''Cosmetic Act,'';

(B) in subparagraph (A)(i), by inserting ''or section 351(k) of this Act'' after ''Cosmetic Act''; and

(C) by amending subparagraph (B) to read as follows:

''(B) there remains no patent listed pursuant to section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act, and every three-year and five-year period referred to in subsection (c)(3)(E)(ii), (c)(3)(E)(iii), (c)(3)(E)(iv), (j)(5)(F)(ii), (j)(5)(F)(iii), or (j)(5)(F)(iv) of section 505 of the Federal Food, Drug, and Cosmetic Act, or applicable twelve-year period

referred to in section 351(k)(7) of this Act, and any seven-year period referred to in section 527 of the Federal Food, Drug, and Cosmetic Act has ended for at least one form of the drug; and''; and

(2) in paragraph (2)—

(A) in the paragraph heading, by striking ''FOR DRUGS LACKING EXCLUSIVITY'';

(B) by striking ''under section 505 of the Federal Food, Drug, and Cosmetic Act''; and

(C) by inserting ''or section 351(m) of this Act,''.

(e) PEDIATRIC SUBCOMMITTEE OF THE ONCOLOGIC ADVISORY COMMITTEE.—Section 15(a) of the Best Pharmaceuticals for Children Act (Public Law 107–109), as amended by section 502(e) of the Food and Drug Administration Amendments Act of 2007 (Public Law 110–85), is amended in paragraph (1)(D), by striking ''section 505B(f)'' and inserting '' 'section 505C' ''.

(f) FOUNDATION OF NATIONAL INSTITUTES OF HEALTH.—Section 499(c)(1)(C) of the Public Health Service Act (42 U.S.C. 290b(c)(1)(C)) is amended by striking ''for which the Secretary issues a certification in the affirmative under section 505A(n)(1)(A) of the Federal Food, Drug, and Cosmetic Act''.

(g) APPLICATION.—Notwithstanding any provision of sections 505A and 505B of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355a, 355c) stating that a provision applies beginning on the date of the enactment of the Best Pharmaceuticals for Children Act of 2007 or the date of the enactment of the Pediatric Research Equity Act of 2007, any amendment made by this Act to such a provision applies beginning on the date of the enactment of this Act.

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