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114TH CONGRESS
2D SESSION

S. 1767

To amend the Federal Food, Drug, and Cosmetic Act with respect to combination products, and for other purposes.

IN THE SENATE OF THE UNITED STATES

JULY 15, 2015

Mr. ISAKSON (for himself, Mr. CASEY, Mr. ROBERTS, Mr. TOOMEY, Mr. KIRK, Mr. DONNELLY, and Mr. CASSIDY) introduced the following bill; which was read twice and referred to the Committee on Health, Education, Labor, and Pensions

APRIL 5, 2016

Reported by Mr. ALEXANDER, with an amendment

[Strike out all after the enacting clause and insert the part printed in italic]

A BILL

To amend the Federal Food, Drug, and Cosmetic Act with respect to combination products, and for other purposes.

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 "Combination Product Regulatory Fairness Act of 2015".~~

SEC. 2. DEVICE DEFINITION.

Section 201(h) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321(h)) is amended—

(1) by redesignating subparagraphs (1), (2), and (3) as clauses (A), (B), and (C), respectively;

(2) by striking ''(h)'' and inserting ''(h)(1)''; and

(3) by adding at the end the following:

''(2)(A) Before determining that an article does not meet the definition of a device under this paragraph, the Secretary shall provide to the sponsor of the article competent and reliable scientific rationale that—

''(i) cites any scientific evidence relied upon to support the rationale; and

''(ii) supports such determination.

''(B) If the Secretary makes a determination described in clause (A)—

''(i) the sponsor of the article may propose a nonclinical or clinical study, limited to not more data than necessary to establish the significance, if any, of the chemical action in achieving the primary intended purpose of the article; and

''(ii) the Secretary and the sponsor of the article shall collaborate in good faith to reach agreement, within a reasonable time not to exceed 90 days, on the design of such study.

''(C) The data resulting from a study conducted under clause (B) shall inform the classification of the article.''.

SEC. 3. COMBINATION PRODUCTS.

Section 503(g) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 353(g)) is amended—

(1) by redesignating paragraphs (2) through (5) as paragraphs (6) through (9), respectively;

(2) by striking ''(g)(1)'' and all that follows through the end of paragraph (1) and inserting the following:

''(g)(1)(A) The Secretary shall, in accordance with this subsection, assign an agency center to regulate products that constitute a combination of a drug, device, or biological product (referred to in this subsection as the 'lead center').

''(B) The Secretary shall conduct the premarket review of any combination product, whenever possible, under a single application using existing premarket review authorities.

''(C) The Secretary shall determine the primary mode of action of the combination product. If the Secretary determines that the primary mode of action is that of—

''(i) a drug (other than a biological product), the agency center charged with premarket review of drugs shall have primary jurisdiction;

''(ii) a device, the agency center charged with premarket review of devices shall have primary jurisdiction; or

''(iii) a biological product, the agency center charged with premarket review of biological products shall have primary jurisdiction.

''(D) In determining the primary mode of action of a combination product, the Secretary shall not determine that the primary mode of action is that of a drug or biological product solely because the combination product has any chemical action within or on the human body.

''(E) If the Secretary disagrees with the conclusions of the sponsor on the primary mode of action of the combination product, the Secretary shall provide a competent and reliable scientific rationale to the product sponsor that cites any scientific evidence relied upon to support the decision.

''(F) For purposes of this paragraph—

''(i) the term 'primary mode of action' means the single mode of action of a combination product that provides the most important therapeutic action of the combination product; and

''(ii) the term 'most important therapeutic action' means the mode of action expected to make the greatest contribution to the overall intended therapeutic effects of the combination product.

''(2)(A) The sponsor of a combination product may submit a combination product review plan (referred to in this subsection as a 'CPRP') for the combination product, and may request a meeting prior to submission of the CPRP, to establish clarity and certainty for the sponsor regarding the standards and requirements applicable to—

''(i) the review of safety and effectiveness, or substantial equivalence, of the combination product;

''(ii) a postmarket modification of the combination product; or

''(iii) good manufacturing practices for the combination product.

''(B) Not later than 60 days after the sponsor of a combination product submits a proposed CPRP, including a revision to a previously proposed or approved CPRP, the Secretary shall review the CPRP and—

''(i) if the Secretary determines that the CPRP is appropriate to ensure adequate review of the safety and effectiveness, or substantial equivalence, of the combination product—

''(I) approve the CPRP; and

‘‘(II) issue to the sponsor a response indicating such approval; or

‘‘(ii) if the Secretary finds that the CPRP does not meet the standard specified in clause (i)—

‘‘(I) decline to approve the CPRP; and

‘‘(II) issue to the sponsor a response indicating that the Secretary has declined such approval and specifying any deficiencies in the proposed CPRP.

‘‘(C)(i) In the case of a CPRP that the Secretary declines to approve under subparagraph (B)(ii), unless the sponsor submitting such CPRP determines a meeting is not necessary, the Secretary shall, not later than 30 days after submitting a response under such subparagraph, meet with such sponsor to discuss the CPRP.

‘‘(ii) A meeting under clause (i) shall—

‘‘(I) include any necessary experts from the relevant agency centers; and

‘‘(II) coordinate the advice of such experts.

‘‘(D) The sponsor or applicant shall provide information necessary for discussion and agreement on the level of evidence necessary to ensure adequate review of the safety and effectiveness, or substantial equivalence, of the combination product.

‘‘(E) Not later than 30 days after the date on which a meeting is held under subparagraph (A)(i), the minutes of such meeting shall be prepared by the sponsor and made available to the Secretary.

‘‘(F) Any agreement that is reached between the Secretary and a sponsor or applicant through a meeting held under subparagraph (A)(i) shall be reduced to writing by the sponsor or applicant, and, once approved by the Secretary, made part of the administrative record by the Secretary within 60 days of such meeting.

‘‘(G) An agreement described in subparagraph (F) shall not be changed after approval of the agreement, except—

‘‘(i) with the written agreement of the sponsor or applicant; or

‘‘(ii) pursuant to a decision, made in accordance with subparagraph (H) by the director of the reviewing division of the lead center, in consultation with consulting centers and the Office, that a substantial scientific issue essential to determining the safety or effectiveness, or substantial equivalence, of the combination product has been identified.

‘‘(H) With respect to a decision under subparagraph (G)(ii), the Secretary shall provide notice, within 2 business days of such decision, to the sponsor of the combina-

tion product and an opportunity for a meeting to take place not later than 14 calendar days after issuing such notice, at which—

"(i) the director of the reviewing division of the lead center, staff from the consulting agency centers, representatives of the Office, and the sponsor will be present; and

"(ii) the director of the reviewing division of the lead center will document the scientific issue involved.

"(3) For purposes of conducting the premarket review of a combination product that contains an approved constituent product described in paragraph (4), the Secretary may require only that the sponsor of such combination product submit to the Secretary data or information that—

"(A) the Secretary determines is necessary to assess the specific safety and effectiveness questions and incremental risks posed by the combination product, using a risk-based approach and taking into account any prior finding of safety and efficacy or substantial equivalence for the approved constituent product; and

"(B) is not duplicative of data or information included in an application or other material sub-

mitted to the Secretary in connection with the approved constituent product.

''(4) For purposes of paragraph (3), an approved constituent product is—

''(A) a drug constituent part of a combination product being reviewed in a single application under section 515 or 510(k), provided such drug constituent part was previously approved under section 505 and such application complies with subparagraph (A) of paragraph (5) and is subject to subparagraphs (D) and (E) of such paragraph;

''(B) a device constituent part approved under section 515 that is referenced by the sponsor and which is available for use by the Secretary under section 520(h)(4); or

''(C) any constituent part that was previously approved, cleared, or licensed under section 505, 510(k), or 515 of this Act or section 351 of the Public Health Service Act, for which the sponsor has a right of reference or which is otherwise available for consideration by the Secretary under this Act or the Public Health Service Act.

''(5)(A) If an application is submitted under section 515 or 510(k) for a combination product containing as a constituent part an approved drug—

~~"(i) the application shall include the certification or statement required pursuant section 505(b)(2); and~~

~~"(ii) the applicant shall provide notice as required pursuant to section 505(b)(3).~~

~~"(B) For purposes of this paragraph, the term 'approved drug' means a drug—~~

~~"(i) that was previously approved under section 505;~~

~~"(ii) for which full reports of investigations that have been made to show whether such drug is safe for use and whether such drug is effective in use—~~

~~"(I) are relied upon by the applicant submitting the application described in subparagraph (A); and~~

~~"(II) were not conducted by or for such applicant; and~~

~~"(iii) with respect to which, the applicant submitting the application described in subparagraph (A) has not obtained a right of reference or use from the person by or for whom the investigations were conducted.~~

~~"(C) The following provisions shall apply with respect an application described in subparagraph (A):~~

"(i) Subparagraphs (A), (B), (C), and (D) of section 505(c)(3).

"(ii) Clauses (ii), (iii), and (iv) of section 505(c)(3)(E).

"(iii) Paragraphs (b) and (c) of section 505A.

"(iv) Section 505E(a).

"(v) Section 527(a).

"(D) Notwithstanding section 520(h)(4)(A)(i), information contained in an application for premarket approval filed with the Secretary pursuant to section 515(c) may not be used to approve any application submitted under section 515 or 510(k) for a combination product containing as a constituent part a drug previously approved under section 505 unless—

"(i) the application includes the certification or statement referenced in subparagraph (A);

"(ii) the applicant provides notice as described in subparagraph (A); and

"(iii) the Secretary's approval of such application is subject to the provisions specified in subparagraph (C).

"(E) An application for a combination product described in subparagraph (A) or (D) shall be considered an application submitted under Section 505(b)(2) solely for purposes of section 271(e)(2)(A) of the Patent Act.";

(3) in paragraph (8) (as redesignated by paragraph (1))—

(A) in subparagraph (C)—

(i) by amending clause (i) to read as follows:

"(i) In carrying out this subsection, the Office shall ensure timely and effective premarket reviews involving more than one agency center by—

"(I) overseeing the timeliness and alignment of reviews; and

"(II) coordinating reviews.";

(ii) in clause (ii), by inserting "and alignment" after "the timeliness" each place it appears; and

(iii) by adding at the end the following new clauses:

"(iii) The Office shall ensure that the lead center be the primary point of contact for the sponsor of the product. The Office shall also coordinate communications to and from any consulting agency center involved in such premarket review. Agency communications and commitments, to the extent consistent with other provisions of law and the requirements of all affected agency centers, from the lead center shall be binding on all other centers involved in the review.

“(iv) The Office shall, with respect to the premarket review of a combination product—

“(I) ensure that any meeting between the Food and Drug Administration and the sponsor of the product is attended by each agency center involved in the review, as appropriate;

“(II) require that each consulting agency center has completed its premarket review and provided the results of such review to the lead center within timeframes that allow the lead center to meet the review goals established pursuant to the most recent authorization or reauthorization of parts 2, 3, 7, and 8, as applicable, of subchapter C of title VII, and

“(III) ensure that each consulting agency center complies with the guidance described in clause (vi) and other relevant regulations, guidances, and policies.

“(v) Not later than 10 days after the receipt by an agency center of an application under section 505, 510(k), or 520 of this Act, or under section 351 of the Public Health Service Act, for a combination product or an application for investigational use of a combination product under section 505(i) or 520(g), the agency center shall inform the Office of such receipt.

''(vi) Not later than 2 years after the date of enactment of the Combination Product Regulatory Fairness Act of 2015, the Secretary shall issue final guidance that describes the responsibilities of each agency center regarding its review of combination products, including each center's role in evaluating evidence development and review under a risk-based approach, dispute resolution, labeling, product usability assessments, and human factors testing. The Office shall, after soliciting public comment, review and update the guidance at least biannually and specify in such updated guidance the reasons for updates.'';

(B) in subparagraph (E)—

(i) by striking clause (i) and inserting the following new clause:

''(i) During the review process, any dispute regarding the substance, timeliness, review process, requirements, or alignment of the premarket review may be presented to the Office for resolution and the Office shall convene the relevant parties and resolve conflicts not later than 90 days after the date on which the Office receives written notice of such conflicts.''; and

(ii) in clause (ii), by striking ''During the review process, any dispute regarding the substance of the premarket review'' and inserting ''Any remaining dispute'';

(C) in subparagraph (F), in the first sentence—

(i) by inserting ''or which involves determining the safety or efficacy of a component of a combination product'' after ''assignment of combination products to agency centers''; and

(ii) by inserting ''and with the guidance described in subparagraph (C)(vi).'' before the period at the end; and

(D) in subparagraph (G)—

(i) in clause (ii), by striking ''and'' at the end;

(ii) in clause (iii), by striking the period at the end and inserting a semicolon; and

(iii) by adding at the end the following new clauses:

''(iv) identifying the percentage of combination products for which a dispute resolution, with respect to premarket review, was requested by the combination product's sponsor; and

''(v) identifying the percentage of meetings between the Food and Drug Administration and the sponsor of a combination product at which all of the

centers participating in the review of the combination product were in attendance, in accordance with subparagraph (C)(iv)(I).'';

(4) in paragraph (9) (as redesignated by paragraph (1)), by adding at the end the following:

''(D) The terms 'premarket review' and 'reviews' include all activities of the Food and Drug Administration conducted prior to approval or clearance of an application or notification submitted under section 505, 510(k), 515, or 520 of this Act or under section 351 of the Public Health Service Act, including with respect to investigational use of the product.''; and

(5) by adding at the end the following:

''(10) RULE OF CONSTRUCTION.—Nothing in this subsection shall be construed as prohibiting a sponsor, at the sponsor's discretion, from submitting separate applications for the constituent parts of a combination product, unless the Secretary determines that a single application is necessary to ensure the safety and effectiveness, or substantial equivalence, as applicable, of the combination product.''.

SECTION 1. SHORT TITLE.

This Act may be cited as the ''Combination Product Regulatory Fairness Act of 2016''.

SEC. 2. COMBINATION PRODUCTS.

(a) IN GENERAL.—Section 503(g) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 353(g)) is amended—

(1) by striking paragraph (3);

(2) by redesignating paragraph (2) as paragraph (7);

(3) by redesignating paragraphs (4) and (5) as paragraphs (8) and (9), respectively; and

(4) by striking "(g)(1)" and all that follows through the end of paragraph (1) and inserting the following:

"(g)(1)(A) The Secretary shall, in accordance with this subsection, assign a primary agency center to regulate products that constitute a combination of a drug, device, or biological product.

"(B) The Secretary shall conduct the premarket review of any combination product under a single application, whenever appropriate.

"(C) For purposes of this subsection, the term 'primary mode of action' means the single mode of action of a combination product expected to make the greatest contribution to the overall intended therapeutic effects of the combination product.

"(D) The Secretary shall determine the primary mode of action of the combination product. If the Secretary determines that the primary mode of action is that of—

"(i) a drug (other than a biological product), the agency center charged with premarket review of drugs shall have primary jurisdiction;

"(ii) a device, the agency center charged with premarket review of devices shall have primary jurisdiction; or

"(iii) a biological product, the agency center charged with premarket review of biological products shall have primary jurisdiction.

"(E) In determining the primary mode of action of a combination product, the Secretary shall not determine that the primary mode of action is that of a drug or biological product solely because the combination product has any chemical action within or on the human body.

"(F) If a sponsor of a combination product disagrees with the determination under subparagraph (D)—

"(i) such sponsor may request, and the Secretary shall provide, a substantive rationale to such sponsor that references scientific evidence provided by the sponsor and any other scientific evidence relied upon by the Secretary to support such determination; and

"(ii)(I) the sponsor of the combination product may propose one or more studies (which may be nonclinical, clinical, or both) to establish the relevance, if

any, of the chemical action in achieving the primary mode of action of such product;

"(II) if the sponsor proposes any such studies, the Secretary and the sponsor of such product shall collaborate and seek to reach agreement, within a reasonable time of such proposal, not to exceed 90 calendar days, on the design of such studies; and

"(III) if an agreement is reached under subclause (II) and the sponsor conducts one or more of such studies, the Secretary shall consider the data resulting from any such study when reevaluating the determination of the primary mode of action of such product, and unless and until such reevaluation has occurred and the Secretary issues a new determination, the determination of the Secretary under subparagraph (D) shall remain in effect.

"(2)(A)(i) To establish clarity and certainty for the sponsor, the sponsor of a combination product may submit a proposed combination product review plan with respect to such combination product, at any point following the Secretary's determination of the primary mode of action pursuant to paragraph (1).

"(ii) Such proposed combination product review plan may—

"(I) address the standards and requirements for market approval or clearance of the combination product;

"(II) address other issues relevant to such combination product, such as requirements related to postmarket modification of such combination product and good manufacturing practices applicable to such combination product; and

"(III) identify elements under subclauses (I) and (II) that may be more appropriate for discussion and agreement with the Secretary at a later date given that scientific or other information is not available, or agreement is otherwise not feasible regarding such elements, at the time such plan is submitted.

"(B) After the sponsor of a combination product submits a proposed combination product review plan under subparagraph (A), the Secretary shall review such plan and, in a written response to such sponsor—

"(i) accept such plan in its entirety, which may include elements to be the subject of discussion and agreement between the sponsor and the Secretary at a later date, as described in subparagraph (A)(ii)(III);

"(ii) accept the plan in part, which may include elements that have not been accepted at the time of the

response and are to be the subject of discussion and agreement between the sponsor and the Secretary at a later date, as described in subparagraph (A)(ii)(III), and elements that the Secretary declines to accept; or

"(iii) deny such plan in its entirety.

"(C) When reviewing a proposed combination product review plan under subparagraph (B), the Secretary shall accept such plan, or elements of such plan, if the Secretary determines that the data to be collected is appropriate—

"(i) for market approval or clearance of the combination product; or

"(ii) to otherwise meet relevant standards under this Act, as applicable.

"(D)(i) If the Secretary declines to accept a proposed combination product review plan under subparagraph (B)(iii), or elements of such a plan under subparagraph (B)(ii), the Secretary shall, in the written response to such sponsor—

"(I) include a description of the deficiencies of such plan or such elements, as applicable; and

"(II) clarify what elements may be suitable for discussion at a later date.

"(ii) If the Secretary declines to accept a proposed combination product review plan under subparagraph

(B)(iii), or elements of such a plan under subparagraph (B)(ii), the sponsor of such plan may request a meeting with the Secretary. Upon the request of the sponsor, the Secretary, including any necessary experts from the relevant agency centers, shall meet with the sponsor to discuss a proposed combination product review plan or elements of a combination product review plan that the Secretary has declined to accept, for the purpose of discussing the information and requirements necessary to make the plan or elements of such plan acceptable. Minutes of such meeting shall be made part of the administrative record.

"(iii) If the Secretary declines to accept a proposed combination product review plan under subparagraph (B)(iii), or elements of such a plan under subparagraph (B)(ii), a sponsor may resubmit a proposed combination product review plan for consideration by the Secretary under subparagraph (A).

"(E) A combination product review plan accepted under subparagraph (B)(i), or the elements of a combination product review plan that are accepted under subparagraph (B)(ii), shall remain in effect, except—

"(i) with the written agreement of the Secretary and the sponsor or applicant; or

"(ii) pursuant to a decision, made in accordance with subparagraph (F) by the director of the review-

ing division of the primary agency center, or a person more senior than such director, in consultation with consulting centers and the Office, that an important, materially relevant scientific issue essential to determining the safety or effectiveness, or substantial equivalence, as applicable, of the combination product has been identified since a combination product review plan or elements of a combination product review plan were accepted, as applicable.

"(F) If the Secretary makes a decision under subparagraph (E)(ii), the Secretary shall provide notice, within a reasonable time after such decision, to the sponsor of the combination product subject to such decision and provide an opportunity for a meeting with the Secretary, to take place within a reasonable time after issuing such notice, at which—

"(i) the director of the reviewing division of the primary agency center, or a person more senior than such director, staff from the consulting centers, representatives of the Office, and the sponsor shall be represented; and

"(ii) the director of the reviewing division of the primary agency center, or a person more senior than the director, shall describe the important, materially relevant issue involved to such sponsor.

"(3) For purposes of conducting the premarket review of a combination product that contains an approved constituent part described in paragraph (4), the Secretary may require that the sponsor of such combination product submit to the Secretary only data or information that the Secretary determines is necessary to assess the safety and effectiveness of the combination product, including any incremental risks and benefits posed by such combination product, using a risk-based approach and taking into account any prior finding of safety and effectiveness or substantial equivalence for the approved constituent part relied upon by the applicant in accordance with paragraph (5).

"(4) For purposes of paragraph (3), an approved constituent part is—

"(A) a drug constituent part of a combination product being reviewed in a single application or request under section 515, 510(k), or 513(f)(2) (submitted in accordance with paragraph (5)), that is an approved drug, provided such application or request complies with paragraph (5);

"(B) a device constituent part approved under section 515 that is referenced by the sponsor and that is available for use by the Secretary under section 520(h)(4); or

"(C) any constituent part that was previously approved, cleared, or classified under section 505, 510(k), 513(f)(2), or 515 of this Act for which the sponsor has a right of reference or any constituent part that is a nonprescription drug, as defined in section 760(a)(2).

"(5)(A) If an application is submitted under section 515, 510(k), or a request is submitted under section 513(f)(2), consistent with any determination made under paragraph (1)(D), for a combination product containing as a constituent part an approved drug—

"(i) the application or request shall include the certification or statement described in section 505(b)(2); and

"(ii) the applicant or requester shall provide notice as described in section 505(b)(3).

"(B) For purposes of this paragraph and paragraph (4), the term 'approved drug' means an active ingredient—

"(i) that was in an application previously approved under section 505(c);

"(ii) where such application is relied upon by the applicant submitting the application or request described in subparagraph (A);

"(iii) for which full reports of investigations that have been made to show whether such drug is safe for

use and whether such drug is effective in use were not conducted by or for the applicant submitting the application or request described in subparagraph (A); and

"(iv) for which the applicant submitting the application or request described in subparagraph (A) has not obtained a right of reference or use from the person by or for whom the investigations described in clause (iii) were conducted.

"(C) The following provisions shall apply with respect to an application or request described in subparagraph (A) to the same extent and in the same manner as if such application or request were an application described in section 505(b)(2) that referenced the approved drug:

"(i) Subparagraphs (A), (B), (C), and (D) of section 505(c)(3).

"(ii) Clauses (ii), (iii), and (iv) of section 505(c)(3)(E).

"(iii) Subsections (b) and (c) of section 505A.

"(iv) Section 505E(a).

"(v) Section 527(a).

"(D) Notwithstanding any other provision of this subsection, an application or request for classification for a combination product described in subparagraph (A) shall be considered an application submitted under section

505(b)(2) for purposes of section 271(e)(2)(A) of title 35, United States Code.

"(6) Nothing in this subsection shall be construed as prohibiting a sponsor from submitting separate applications for the constituent parts of a combination product, unless the Secretary determines that a single application is necessary.";

(5) in paragraph (8) (as redesignated by paragraph (3))—

(A) in subparagraph (C)—

(i) by amending clause (i) to read as follows:

"(i) In carrying out this subsection, the Office shall help to ensure timely and effective premarket review that involves more than one agency center by coordinating such reviews, overseeing the timeliness of such reviews, and overseeing the alignment of feedback regarding such reviews.";

(ii) in clause (ii), by inserting "and alignment" after "the timeliness" each place it appears; and

(iii) by adding at the end the following new clauses:

"(iii) The Office shall ensure that, with respect to a combination product, a designated person or persons in the primary agency center be the primary point or points of

contact for the sponsor of such combination product. The Office shall also coordinate communications to and from any consulting center involved in such premarket review, if requested by such primary agency center or any such consulting center. Agency communications and commitments, to the extent consistent with other provisions of law and the requirements of all affected agency centers, from the primary agency center shall be considered as communication from the Food and Drug Administration on behalf of all agency centers involved in the review.

"(iv) The Office shall, with respect to the premarket review of a combination product—

"(I) ensure that any meeting between the Food and Drug Administration and the sponsor of such product is attended by each agency center involved in the review, as appropriate;

"(II) ensure that each consulting agency center has completed its premarket review and provided the results of such review to the primary agency center in a timely manner; and

"(III) ensure that each consulting center follows the guidance described in clause (vi) and advises, as appropriate, on other relevant regulations, guidances, and policies.

"(v) In seeking agency action with respect to a combination product, the sponsor of such product—

"(I) shall identify the product as a combination product; and

"(II) may request in writing the participation of representatives of the Office in meetings related to such combination product, or to have the Office otherwise engage on such regulatory matters concerning the combination product.

"(vi) Not later than 4 years after the date of enactment of the Combination Product Regulatory Fairness Act of 2016, and after a public comment period of not less than 60 calendar days, the Secretary shall issue a final guidance that describes—

"(I) the responsibilities of each agency center regarding its review of combination products, including each center's role in evaluating evidence development and review under a risk-based approach, dispute resolution, labeling, product usability assessments, and human factors testing;

"(II) the structured process for managing pre-submission interactions with sponsors developing combination products;

"(III) the best practices for ensuring that the feedback in such pre-submission interactions rep-

resents the Agency's best advice based on the information provided during such pre-submission interactions;

"(IV) the best practices regarding submissions by sponsors, and review by the Secretary, of combination product review plans under paragraph (2), including the appropriate timing for discussion and agreement of such plans, and the various elements of such plans, based on scientific and technical understanding during product development;

"(V) the Secretary's processes for ensuring input from experts from each relevant agency center in such pre-submission interactions with sponsors developing combination products and in fulfilling the requirements of this subsection;

"(VI) the timelines associated with responding to, and holding meetings regarding, combination product review plans under paragraph (2); and

"(VII) disputes appropriate for presentation to the Office as described in subparagraph (E)(i).".

(B) in subparagraph (E)—

(i) by striking clause (i) and inserting the following new clause:

"(i) During the review process, disputes between different agency centers regarding the substance, timeliness, re-

view process, requirements, or alignment of the premarket review with respect to a combination product, including conflicting feedback, responses, and decisions from such agency centers, may be presented to the Office by the sponsor of such combination product for resolution and the Office shall convene the relevant parties and seek to resolve such conflicts.''; and

(ii) in clause (ii), by striking ''During the review process, any dispute regarding the substance of the premarket review'' and inserting ''Any dispute remaining after the process under clause (i) is completed'';

(C) in subparagraph (F), in the first sentence—

(i) by inserting ''or that involves determining the safety or efficacy, reasonable assurance of safety and efficacy, or substantial equivalence of a component of a combination product'' after ''assignment of combination products to agency centers''; and

(ii) by inserting ''and with the guidance described in subparagraph (C)(vi)'' before the period at the end; and

(D) in subparagraph (G)—

(i) in clause (ii), by striking "and" at the end;

(ii) in clause (iii), by striking the period at the end and inserting a semicolon; and

(iii) by adding at the end the following new clauses:

"(iv) identifying the percentage of combination products for which a dispute resolution, with respect to premarket review, was requested by the combination product's sponsor;

"(v) stating the average, median, and range of response times to combination product review plans under paragraph (2);

"(vi) identifying the percentage of meetings between the Food and Drug Administration and the sponsor of a combination product at which all of the agency centers participating in the review of the combination product were in attendance, in accordance with subparagraph (C)(iv)(I); and

"(vii) for the report submitted in 2017, and in a report at least once every 5 years thereafter, regarding any recommendations to streamline premarket review of combination products."; and

(6) in paragraph (9) (as redesignated by paragraph (3))—

(A) in subparagraph (C)—

(i) in clause (ii), by striking "and";

(ii) in clause (iii), by striking the period and inserting ", and"; and

(iii) by adding at the end the following:

"(iv) de novo classification under section 513(a)(1)."; and

(B) by adding at the end the following:

"(D) The terms 'premarket review' and 'reviews' include all activities of the Food and Drug Administration conducted prior to approval or clearance of an application, notification, or request for classification submitted under section 505, 510(k), 513(f)(2), 515, or 520 of this Act or under section 351 of the Public Health Service Act, including with respect to investigational use of the product.".

(b) INFORMATION FOR APPROVAL OF COMBINATION PRODUCTS.—Section 520(h)(4) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360j) is amended—

(1) in subparagraph (A), by striking "Any information" and inserting "Subject to subparagraph (C), any information"; and

(2) by adding at the end the following new subparagraph:

"(C) No information contained in an application for premarket approval filed with the Secretary pursuant to section 515(c) may be used to approve or clear any application submitted under section 515 or 510(k) or to classify a product under section 513(f)(2) for a combination product containing as a constituent part an "approved drug" as defined in section 503(g)(5)(B) unless—

"(i) the application includes the certification or statement referenced in section 503(g)(5)(A);

"(ii) the applicant provides notice as described in Section 503(g)(5)(A); and

"(iii) the Secretary's approval of such application is subject to the provisions in section 503(g)(5)(C).".

(c) VARIATIONS FROM CGMP STREAMLINED APPROACH.—Not later than 18 months after the date of enactment of this Act, the Secretary shall identify types of combination products that the Secretary proposes may adopt good manufacturing practices that vary from the requirements set forth in section 4.4 of title 21, Code of Federal

Regulations (or any successor regulations). The Secretary shall identify such types, and identify variations from such requirements, in a proposed list published in the Federal Register. After a public comment period regarding the appropriate good manufacturing practices for such types, the Secretary shall publish a final list in the Federal Register, notwithstanding section 553 of title 5, United States Code. The Secretary shall evaluate such types and such appropriate variations using a risk-based approach. The Secretary shall periodically review such types on such final list, including whether additional types of combination products are appropriate for such final list.

Calendar No. 414

114TH CONGRESS
2D SESSION

S. 1767

A BILL

To amend the Federal Food, Drug, and Cosmetic Act with respect to combination products, and for other purposes.

APRIL 5, 2016

Reported with an amendment