114TH CONGRESS
1ST SESSION

S. _____

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

Mr. ISAKSON (for himself, Mr. CASEY, and Mr. ROBERTS) introduced the following bill; which was read twice and referred to the Committee on _____

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 "_____ 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; and

(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 combination 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 submitted 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; and

"(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 [_____ 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 combina-

tion 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.''.