Monday 5:39pm
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AMENDMENT

OFFERED BY MS. ESHOO OF CALIFORNIA, MR. INSLEE OF WASHINGTON, AND MR. BARTON OF TEXAS

At the end of title V of division C, add the following:

Subtitle ____—Pathway for Biosimilars

SEC. ___. LICENSURE PATHWAY FOR BIOSIMILAR BIOLOGICAL PRODUCTS.

(a) LICENSURE OF BIOLOGICAL PRODUCTS AS BIOSIMILAR OR INTERCHANGEABLE.—Section 351 of the Public Health Service Act (42 U.S.C. 262) is amended—

(1) in subsection (a)(1)(A), by inserting "under this subsection or subsection (k)" after "biologics license"; and

(2) by adding at the end the following:

"(k) LICENSURE OF BIOLOGICAL PRODUCTS AS BIOSIMILAR OR INTERCHANGEABLE.—

"(1) IN GENERAL.—Any person may submit an application for licensure of a biological product under this subsection.

"(2) CONTENT.—

"(A) IN GENERAL.—

"(i) REQUIRED INFORMATION.—An application submitted under this subsection shall include information demonstrating that—

"(I) the biological product is biosimilar to a reference product based upon data derived from—

"(aa) analytical studies that demonstrate that the biological product is highly similar to the reference product notwithstanding minor differences in clinically inactive components;

"(bb) animal studies (including the assessment of toxicity); and

"(cc) a clinical study or studies (including the assessment of immunogenicity and pharmacokinetics or pharmacodynamics) that are sufficient to demonstrate safety, purity, and potency in 1 or more appropriate conditions of use for which the reference product is li-

censed and intended to be used and for which licensure is sought for the biological product;

"(II) the biological product and reference product utilize the same mechanism or mechanisms of action for the condition or conditions of use prescribed, recommended, or suggested in the proposed labeling, but only to the extent the mechanism or mechanisms of action are known for the reference product;

"(III) the condition or conditions of use prescribed, recommended, or suggested in the labeling proposed for the biological product have been previously approved for the reference product;

"(IV) the route of administration, the dosage form, and the strength of the biological product are the same as those of the reference product; and

"(V) the facility in which the biological product is manufactured, proc-

essed, packed, or held meets standards designed to assure that the biological product continues to be safe, pure, and potent.

"(ii) DETERMINATION BY SECRETARY.—The Secretary may determine, in the Secretary's discretion, that an element described in clause (i)(I) is unnecessary in an application submitted under this subsection.

"(iii) ADDITIONAL INFORMATION.—An application submitted under this subsection—

"(I) shall include publicly-available information regarding the Secretary's previous determination that the reference product is safe, pure, and potent; and

"(II) may include any additional information in support of the application, including publicly-available information with respect to the reference product or another biological product.

"(B) INTERCHANGEABILITY.—An application (or a supplement to an application) sub-

mitted under this subsection may include information demonstrating that the biological product meets the standards described in paragraph (4).

"(3) EVALUATION BY SECRETARY.—Upon review of an application (or a supplement to an application) submitted under this subsection, the Secretary shall license the biological product under this subsection if—

"(A) the Secretary determines that the information submitted in the application (or the supplement) is sufficient to show that the biological product—

"(i) is biosimilar to the reference product; or

"(ii) meets the standards described in paragraph (4), and therefore is interchangeable with the reference product; and

"(B) the applicant (or other appropriate person) consents to the inspection of the facility that is the subject of the application, in accordance with subsection (c).

"(4) SAFETY STANDARDS FOR DETERMINING INTERCHANGEABILITY.—Upon review of an application submitted under this subsection or any supple-

ment to such application, the Secretary shall determine the biological product to be interchangeable with the reference product if the Secretary determines that the information submitted in the application (or a supplement to such application) is sufficient to show that—

"(A) the biological product—

"(i) is biosimilar to the reference product; and

"(ii) can be expected to produce the same clinical result as the reference product in any given patient; and

"(B) for a biological product that is administered more than once to an individual, the risk in terms of safety or diminished efficacy of alternating or switching between use of the biological product and the reference product is not greater than the risk of using the reference product without such alternation or switch.

"(5) GENERAL RULES.—

"(A) ONE REFERENCE PRODUCT PER APPLICATION.—A biological product, in an application submitted under this subsection, may not be evaluated against more than 1 reference product.

"(B) REVIEW.—An application submitted under this subsection shall be reviewed by the division within the Food and Drug Administration that is responsible for the review and approval of the application under which the reference product is licensed.

"(C) RISK EVALUATION AND MITIGATION STRATEGIES.—The authority of the Secretary with respect to risk evaluation and mitigation strategies under the Federal Food, Drug, and Cosmetic Act shall apply to biological products licensed under this subsection in the same manner as such authority applies to biological products licensed under subsection (a).

"(D) RESTRICTIONS ON BIOLOGICAL PRODUCTS CONTAINING DANGEROUS INGREDIENTS.—If information in an application submitted under this subsection, in a supplement to such an application, or otherwise available to the Secretary shows that a biological product—

"(i) is, bears, or contains a select agent or toxin listed in section 73.3 or 73.4 of title 42, section 121.3 or 121.4 of title 9, or section 331.3 of title 7, Code of

Federal Regulations (or any successor regulations); or

"(ii) is, bears, or contains a controlled substance in schedule I or II of section 202 of the Controlled Substances Act, as listed in part 1308 of title 21, Code of Federal Regulations (or any successor regulations);

the Secretary shall not license the biological product under this subsection unless the Secretary determines, after consultation with appropriate national security and drug enforcement agencies, that there would be no increased risk to the security or health of the public from licensing such biological product under this subsection.

"(6) EXCLUSIVITY FOR FIRST INTERCHANGEABLE BIOLOGICAL PRODUCT.—Upon review of an application submitted under this subsection relying on the same reference product for which a prior biological product has received a determination of interchangeability for any condition of use, the Secretary shall not make a determination under paragraph (4) that the second or subsequent biological product is

interchangeable for any condition of use until the earlier of—

"(A) 1 year after the first commercial marketing of the first interchangeable biosimilar biological product to be approved as interchangeable for that reference product;

"(B) 18 months after—

"(i) a final court decision on all patents in suit in an action instituted under subsection (l)(5) against the applicant that submitted the application for the first approved interchangeable biosimilar biological product; or

"(ii) the dismissal with or without prejudice of an action instituted under subsection (l)(5) against the applicant that submitted the application for the first approved interchangeable biosimilar biological product; or

"(C)(i) 42 months after approval of the first interchangeable biosimilar biological product if the applicant that submitted such application has been sued under subsection (l)(5) and such litigation is still ongoing within such 42-month period; or

"(ii) 18 months after approval of the first interchangeable biosimilar biological product if the applicant that submitted such application has not been sued under subsection (l)(5).

For purposes of this paragraph, the term 'final court decision' means a final decision of a court from which no appeal (other than a petition to the United States Supreme Court for a writ of certiorari) has been or can be taken.

"(7) EXCLUSIVITY FOR REFERENCE PRODUCT.—

"(A) EFFECTIVE DATE OF BIOSIMILAR APPLICATION APPROVAL.—Approval of an application under this subsection may not be made effective by the Secretary until the date that is 12 years after the date on which the reference product was first licensed under subsection (a).

"(B) FILING PERIOD.—An application under this subsection may not be submitted to the Secretary until the date that is 4 years after the date on which the reference product was first licensed under subsection (a).

"(C) FIRST LICENSURE.—Subparagraphs (A) and (B) shall not apply to a license for or approval of—

"(i) a supplement for the biological product that is the reference product; or

"(ii) a subsequent application filed by the same sponsor or manufacturer of the biological product that is the reference product (or a licensor, predecessor in interest, or other related entity) for—

"(I) a change (not including a modification to the structure of the biological product) that results in a new indication, route of administration, dosing schedule, dosage form, delivery system, delivery device, or strength; or

"(II) a modification to the structure of the biological product that does not result in a change in safety, purity, or potency.

"(8) PEDIATRIC STUDIES.—

"(A) EXCLUSIVITY.—If, before or after licensure of the reference product under subsection (a) of this section, the Secretary determines that information relating to the use of such product in the pediatric population may produce health benefits in that population, the Secretary makes a written request for pediatric

studies (which shall include a timeframe for completing such studies), the applicant or holder of the approved application agrees to the request, such studies are completed using appropriate formulations for each age group for which the study is requested within any such timeframe, and the reports thereof are submitted and accepted in accordance with section 505A(d)(3) of the Federal Food, Drug, and Cosmetic Act the period referred to in paragraph (7)(A) of this subsection is deemed to be 12 years and 6 months rather than 12 years.

"(B) EXCEPTION.—The Secretary shall not extend the period referred to in subparagraph (A) of this paragraph if the determination under section 505A(d)(3) of the Federal Food, Drug, and Cosmetic Act is made later than 9 months prior to the expiration of such period.

"(C) APPLICATION OF CERTAIN PROVISIONS.—The provisions of subsections (a), (d), (e), (f), (h), (j), (k), and (l) of section 505A of the Federal Food, Drug, and Cosmetic Act shall apply with respect to the extension of a period under subparagraph (A) of this para-

graph to the same extent and in the same manner as such provisions apply with respect to the extension of a period under subsection (b) or (c) of section 505A of the Federal Food, Drug, and Cosmetic Act.

"(9) GUIDANCE DOCUMENTS.—

"(A) IN GENERAL.—The Secretary may, after opportunity for public comment, issue guidance in accordance, except as provided in subparagraph (B)(i), with section 701(h) of the Federal Food, Drug, and Cosmetic Act with respect to the licensure of a biological product under this subsection. Any such guidance may be general or specific.

"(B) PUBLIC COMMENT.—

"(i) IN GENERAL.—The Secretary shall provide the public an opportunity to comment on any proposed guidance issued under subparagraph (A) before issuing final guidance.

"(ii) INPUT REGARDING MOST VALUABLE GUIDANCE.—The Secretary shall establish a process through which the public may provide the Secretary with input regarding priorities for issuing guidance.

"(C) NO REQUIREMENT FOR APPLICATION CONSIDERATION.—The issuance (or non-issuance) of guidance under subparagraph (A) shall not preclude the review of, or action on, an application submitted under this subsection.

"(D) REQUIREMENT FOR PRODUCT CLASS-SPECIFIC GUIDANCE.—If the Secretary issues product class-specific guidance under subparagraph (A), such guidance shall include a description of—

"(i) the criteria that the Secretary will use to determine whether a biological product is highly similar to a reference product in such product class; and

"(ii) the criteria, if available, that the Secretary will use to determine whether a biological product meets the standards described in paragraph (4).

"(E) CERTAIN PRODUCT CLASSES.—

"(i) GUIDANCE.—The Secretary may indicate in a guidance document that the science and experience, as of the date of such guidance, with respect to a product or product class (not including any recombinant protein) does not allow approval of

an application for a license as provided under this subsection for such product or product class.

"(ii) MODIFICATION OR REVERSAL.—The Secretary may issue a subsequent guidance document under subparagraph (A) to modify or reverse a guidance document under clause (i).

"(iii) NO EFFECT ON ABILITY TO DENY LICENSE.—Clause (i) shall not be construed to require the Secretary to approve a product with respect to which the Secretary has not indicated in a guidance document that the science and experience, as described in clause (i), does not allow approval of such an application.

"(10) NAMING.—The Secretary shall ensure that the labeling and packaging of each biological product licensed under this subsection bears a name that uniquely identifies the biological product and distinguishes it from the reference product and any other biological products licensed under this subsection following evaluation against such reference product.

"(l) PATENT NOTICES; RELATIONSHIP TO FINAL APPROVAL.—

"(1) DEFINITIONS.—For the purposes of this subsection, the term—

"(A) 'biosimilar product' means the biological product that is the subject of the application under subsection (k);

"(B) 'relevant patent' means a patent that—

"(i) expires after the date specified in subsection (k)(7)(A) that applies to the reference product; and

"(ii) could reasonably be asserted against the applicant due to the unauthorized making, use, sale, or offer for sale within the United States, or the importation into the United States of the biosimilar product, or materials used in the manufacture of the biosimilar product, or due to a use of the biosimilar product in a method of treatment that is indicated in the application;

"(C) 'reference product sponsor' means the holder of an approved application or license for the reference product; and

"(D) 'interested third party' means a person other than the reference product sponsor that owns a relevant patent, or has the right to commence or participate in an action for infringement of a relevant patent.

"(2) HANDLING OF CONFIDENTIAL INFORMATION.—Any entity receiving confidential information pursuant to this subsection shall designate one or more individuals to receive such information. Each individual so designated shall execute an agreement in accordance with regulations promulgated by the Secretary. The regulations shall require each such individual to take reasonable steps to maintain the confidentiality of information received pursuant to this subsection and use the information solely for purposes authorized by this subsection. The obligations imposed on an individual who has received confidential information pursuant to this subsection shall continue until the individual returns or destroys the confidential information, a court imposes a protective order that governs the use or handling of the confidential information, or the party providing the confidential information agrees to other terms or conditions regarding the handling or use of the confidential information.

"(3) PUBLIC NOTICE BY SECRETARY.—Within 30 days of acceptance by the Secretary of an application filed under subsection (k), the Secretary shall publish a notice identifying—

"(A) the reference product identified in the application; and

"(B) the name and address of an agent designated by the applicant to receive notices pursuant to paragraph (4)(B).

"(4) EXCHANGES CONCERNING PATENTS.—

"(A) EXCHANGES WITH REFERENCE PRODUCT SPONSOR.—

"(i) Within 30 days of the date of acceptance of the application by the Secretary, the applicant shall provide the reference product sponsor with a copy of the application and information concerning the biosimilar product and its production. This information shall include a detailed description of the biosimilar product, its method of manufacture, and the materials used in the manufacture of the product.

"(ii) Within 60 days of the date of receipt of the information required to be provided under clause (i), the reference prod-

uct sponsor shall provide to the applicant a list of relevant patents owned by the reference product sponsor, or in respect of which the reference product sponsor has the right to commence an action of infringement or otherwise has an interest in the patent as such patent concerns the biosimilar product.

"(iii) If the reference product sponsor is issued or acquires an interest in a relevant patent after the date on which the reference product sponsor provides the list required by clause (ii) to the applicant, the reference product sponsor shall identify that patent to the applicant within 30 days of the date of issue of the patent, or the date of acquisition of the interest in the patent, as applicable.

"(B) EXCHANGES WITH INTERESTED THIRD PARTIES.—

"(i) At any time after the date on which the Secretary publishes a notice for an application under paragraph (3), any interested third party may provide notice to the designated agent of the applicant

that the interested third party owns or has rights under 1 or more patents that may be relevant patents. The notice shall identify at least 1 patent and shall designate an individual who has executed an agreement in accordance with paragraph (2) to receive confidential information from the applicant.

"(ii) Within 30 days of the date of receiving notice pursuant to clause (i), the applicant shall send to the individual designated by the interested third party the information specified in subparagraph (A)(i), unless the applicant and interested third party otherwise agree.

"(iii) Within 90 days of the date of receiving information pursuant to clause (ii), the interested third party shall provide to the applicant a list of relevant patents which the interested third party owns, or in respect of which the interested third party has the right to commence or participate in an action for infringement.

"(iv) If the interested third party is issued or acquires an interest in a relevant

patent after the date on which the interested third party provides the list required by clause (iii), the interested third party shall identify that patent within 30 days of the date of issue of the patent, or the date of acquisition of the interest in the patent, as applicable.

"(C) IDENTIFICATION OF BASIS FOR INFRINGEMENT.—For any patent identified under clause (ii) or (iii) of subparagraph (A) or under clause (iii) or (iv) of subparagraph (B), the reference product sponsor or the interested third party, as applicable—

"(i) shall explain in writing why the sponsor or the interested third party believes the relevant patent would be infringed by the making, use, sale, or offer for sale within the United States, or importation into the United States, of the biosimilar product or by a use of the biosimilar product in treatment that is indicated in the application;

"(ii) may specify whether the relevant patent is available for licensing; and

"(iii) shall specify the number and date of expiration of the relevant patent.

"(D) CERTIFICATION BY APPLICANT CONCERNING IDENTIFIED RELEVANT PATENTS.—Not later than 45 days after the date on which a patent is identified under clause (ii) or (iii) of subparagraph (A) or under clause (iii) or (iv) of subparagraph (B), the applicant shall send a written statement regarding each identified patent to the party that identified the patent. Such statement shall either—

"(i) state that the applicant will not commence marketing of the biosimilar product and has requested the Secretary to not grant final approval of the application before the date of expiration of the noticed patent; or

"(ii) provide a detailed written explanation setting forth the reasons why the applicant believes—

"(I) the making, use, sale, or offer for sale within the United States, or the importation into the United States, of the biosimilar product, or the use of the biosimilar prod-

uct in a treatment indicated in the application, would not infringe the patent; or

"(II) the patent is invalid or unenforceable.

"(5) ACTION FOR INFRINGEMENT INVOLVING REFERENCE PRODUCT SPONSOR.—If an action for infringement concerning a relevant patent identified by the reference product sponsor under clause (ii) or (iii) of paragraph (4)(A), or by an interested third party under clause (iii) or (iv) of paragraph (4)(B), is brought within 60 days of the date of receipt of a statement under paragraph (4)(D)(ii), and the court in which such action has been commenced determines the patent is infringed prior to the date applicable under subsection (k)(7)(A) or (k)(8), the Secretary shall make approval of the application effective on the day after the date of expiration of the patent that has been found to be infringed. If more than one such patent is found to be infringed by the court, the approval of the application shall be made effective on the day after the date that the last such patent expires.".

(b) DEFINITIONS.—Section 351(i) of the Public Health Service Act (42 U.S.C. 262(i)) is amended—

(1) by striking "In this section, the term 'biological product' means" and inserting the following: "In this section:

"(1) The term 'biological product' means";

(2) in paragraph (1), as so designated, by inserting "protein (except any chemically synthesized polypeptide)," after "allergenic product,"; and

(3) by adding at the end the following:

"(2) The term 'biosimilar' or 'biosimilarity', in reference to a biological product that is the subject of an application under subsection (k), means—

"(A) that the biological product is highly similar to the reference product notwithstanding minor differences in clinically inactive components; and

"(B) there are no clinically meaningful differences between the biological product and the reference product in terms of the safety, purity, and potency of the product.

"(3) The term 'interchangeable' or 'interchangeability', in reference to a biological product that is shown to meet the standards described in subsection (k)(4), means that the biological product may be substituted for the reference product without

the intervention of the health care provider who prescribed the reference product.

"(4) The term 'reference product' means the single biological product licensed under subsection (a) against which a biological product is evaluated in an application submitted under subsection (k).".

(c) PRODUCTS PREVIOUSLY APPROVED UNDER SECTION 505.—

(1) REQUIREMENT TO FOLLOW SECTION 351.—Except as provided in paragraph (2), an application for a biological product shall be submitted under section 351 of the Public Health Service Act (42 U.S.C. 262) (as amended by this Act).

(2) EXCEPTION.—An application for a biological product may be submitted under section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355) if—

(A) such biological product is in a product class for which a biological product in such product class is the subject of an application approved under such section 505 not later than the date of enactment of this Act; and

(B) such application—

(i) has been submitted to the Secretary of Health and Human Services (re-

ferred to in this Act as the "Secretary") before the date of enactment of this Act; or

(ii) is submitted to the Secretary not later than the date that is 10 years after the date of enactment of this Act.

(3) LIMITATION.—Notwithstanding paragraph (2), an application for a biological product may not be submitted under section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355) if there is another biological product approved under subsection (a) of section 351 of the Public Health Service Act that could be a reference product with respect to such application (within the meaning of such section 351) if such application were submitted under subsection (k) of such section 351.

(4) DEEMED APPROVED UNDER SECTION 351.—An approved application for a biological product under section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355) shall be deemed to be a license for the biological product under such section 351 on the date that is 10 years after the date of enactment of this Act.

(5) DEFINITIONS.—For purposes of this subsection, the term "biological product" has the mean-

ing given such term under section 351 of the Public Health Service Act (42 U.S.C. 262) (as amended by this Act).

SEC. ___. FEES RELATING TO BIOSIMILAR BIOLOGICAL PRODUCTS.

Subparagraph (B) of section 735(1) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 379g(1)) is amended by inserting ", including licensure of a biological product under section 351(k) of such Act" before the period at the end.

AGENDA ITEM # 21 ADDENDUM
8/19-20/09 ICOC MEETING
PASSED 47-11 ON 7/31/09 BY HOUSE ENERGY AND COMMERCE COMMITTEE