I

111TH CONGRESS
1ST SESSION

H. R. 1548

To amend the Public Health Service Act to establish a pathway for the licensure of biosimilar biological products, and for other purposes.

IN THE HOUSE OF REPRESENTATIVES

MARCH 17, 2009

Ms. ESHOO (for herself, Mr. INSLEE, Mr. BARTON of Texas, Mr. GENE GREEN of Texas, Ms. BALDWIN, Mr. ROGERS of Michigan, Mrs. BONO MACK, Mr. HILL, Mr. UPTON, Mr. BARROW, Mr. PITTS, Mr. THOMPSON of California, Mr. CAPUANO, Mrs. DAVIS of California, Mr. BILBRAY, Mr. DREIER, Mr. ELLSWORTH, Mr. MCGOVERN, Mr. HERGER, Mr. DENT, Mr. GERLACH, Mr. BISHOP of New York, Ms. ZOE LOFGREN of California, Mr. PENCE, Mr. SOUDER, Mr. HONDA, Mrs. TAUSCHER, Mr. SCALISE, Mr. TOWNS, Mr. CROWLEY, Mr. ISSA, Mr. PATRICK J. MURPHY of Pennsylvania, Ms. BEAN, Mr. DELAHUNT, Mr. SMITH of Washington, Mr. MCCARTHY of California, Mr. NEAL of Massachusetts, Mr. LYNCH, Mr. DONNELLY of Indiana, Mr. HALL of Texas, Mr. LANCE, Mr. HOLT, Mr. NUNES, and Mr. KIND) introduced the following bill; which was referred to the Committee on Energy and Commerce, and in addition to the Committee on the Judiciary, for a period to be subsequently determined by the Speaker, in each case for consideration of such provisions as fall within the jurisdiction of the committee concerned

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A BILL

To amend the Public Health Service Act to establish a pathway for the licensure of biosimilar biological 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 ''Pathway for Biosimilars Act''.

SEC. 2. TABLE OF CONTENTS.

The table of contents for this Act is as follows:

TITLE I—AMENDMENTS TO PUBLIC HEALTH SERVICE ACT

SEC. 101. 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.—

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

''(2) CONTENT.—

''(A) 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—

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

''(II) animal studies (including the assessment of toxicity); and

''(III) a clinical study or studies (including, but not limited to, the assessment of immunogenicity and pharmacokinetics or pharmacodynamics) that are sufficient to demonstrate safety, purity, and potency for each condition of use for which the reference product is approved;

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

''(B) WAIVER REGARDING ANALYTICAL STUDIES, ANIMAL STUDIES, AND CLINICAL STUDIES.—

''(i) IN GENERAL.—The Secretary may, in the Secretary's discretion, determine that an element described in sub-

clause (I), (II), or (III) of subparagraph (A)(i) is unnecessary and waive the requirement that such element be submitted in an application under this subsection.

''(ii) ASSESSMENTS OF IMMUNOGENICITY.—Notwithstanding clause (i), the Secretary may determine that an assessment of immunogenicity described in subparagraph (A)(i)(III) is unnecessary and waive the requirement that such an assessment be submitted in an application under this subsection only if the Secretary has published a final guidance, following receipt and consideration of public comments on a draft guidance—

''(I) advising that it is feasible in the current state of scientific knowledge to make determinations on immunogenicity with respect to products in the product class to which the biological product belongs; and

''(II) explaining the data that will be required to support such a determination.

''(C) 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.

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

''(A) the Secretary determines that the information submitted in the application (or the supplement) is sufficient to show that the biological product is biosimilar to the reference product with respect to each condition of use for which the reference product is approved; 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.—

''(A) DETERMINATION.—Upon review of an application submitted under this subsection or any supplement 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—

''(i) the biological product—

''(I) is biosimilar to the reference product and any biological product licensed under this subsection that has been determined to be interchangeable with the reference product; and

''(II) can be expected to produce the same clinical result as the reference product in any given patient for each condition of use prescribed, recommended, or suggested in the labeling of the reference product; and

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

"(B) GUIDELINES.—Notwithstanding subparagraph (A), the Secretary may not make a determination that a biological product licensed under this subsection is interchangeable with the reference product unless the Secretary has published a final guidance, following receipt and consideration of public comments on a draft guidance—

"(i) advising that it is feasible in the current state of scientific knowledge to make such determinations with respect to products in the product class to which that biological product belongs; and

"(ii) explaining the data that will be required to support such a determination.

"(C) PRESERVATION OF STATE AUTHORITY.—Nothing in this subsection shall be construed as preempting or otherwise affecting the authority of a State to require or regulate prescriptions.

"(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.—The Secretary shall not make a determination under paragraph (4) that a second or subsequent biological product is interchangeable with the same reference product for which a prior biological product has received a determination of interchangeability until 24 months after the later of—

''(A) the date of the first commercial marketing of the first biosimilar biological product determined to be interchangeable for that reference product; or

''(B) with respect to a product marketed before the date the product is determined to be interchangeable, the date that the product is determined to be interchangeable.

''(7) EXCLUSIVITY FOR REFERENCE PRODUCT.—

''(A) EFFECTIVE DATE OF BIOSIMILAR APPLICATION LICENSURE.—Subject to subparagraph (D) and paragraph (8), 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 later of—

"(i) the date of commencement of a proceeding for issuance of guidance pursuant to paragraph (9) with respect to the product class within which the product that is the subject of such application falls; or

"(ii) the date that is 4 years after the date on which the reference product was first licensed under subsection (a).

"(C) FIRST LICENSURE.—For purposes of this paragraph, the date on which the reference product was first licensed under subsection (a) does not include the date of approval of a supplement or of a subsequent application for a new indication, route of administration, dosage form, or strength for the previously licensed reference product.

"(D) MEDICALLY SIGNIFICANT NEW INDICATION.—If, during the 8-year period following

licensure of the reference product, the Secretary approves a supplement to the application for the reference product that seeks approval to market the reference product for a new indication that, if approved, would be a significant improvement, compared to marketed products, in the treatment, diagnosis, or prevention of disease, approval of an application submitted under this subsection may not be made effective by the Secretary until the date that is 14 years after the date on which the reference product was first licensed under subsection (a).

''(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—

"(i) the period referred to in paragraph (7)(A) of this subsection is deemed to be 12 years and 6 months rather than 12 years; and

"(ii) if paragraph (7)(D) of this subsection applies, the period referred to in such paragraph is deemed to be 14 years and 6 months rather than 14 years.

"(B) EXCEPTION.—The Secretary shall not extend the period referred to in subparagraph (A)(i) or (A)(ii) 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 paragraph 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 shall, after opportunity for public comment, issue final guidance with respect to the licensure under this subsection of a biological product or product class. Such guidance shall be issued in accordance, except as provided in subparagraph (B)(i), with section 701(h) of the Federal Food, Drug, and Cosmetic Act.

''(B) PUBLIC COMMENT.—

''(i) IN GENERAL.—Before issuing final guidance under subparagraph (A), the Secretary shall publish a proposed guidance, provide an opportunity for the public to comment on the proposed guidance, and publish a response to comments received under this clause.

''(ii) INPUT REGARDING MOST VALUABLE GUIDANCE.—The Secretary shall es-

tablish a process through which the public may provide the Secretary with input regarding priorities for issuing guidance.

''(C) CERTAIN PRODUCT CLASSES.—

''(i) GUIDANCE.—The Secretary may indicate in a guidance document under subparagraph (A) that the Secretary will not license a product or product class (not including any recombinant protein) under this subsection because the science and experience, as of the date of such guidance, does not allow such licensure.

''(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).

''(D) PETITION FOR INITIATION OF GUIDANCE FOR CERTAIN PRODUCTS.—In the case of a reference product that was licensed by the Secretary more than 7 years prior to the date of the enactment of the Pathway for Biosimilars Act, a person may petition the Secretary at any time to commence the process for issuing final guidance under subparagraph (A)

for the product class to which the reference product belongs. Any such petition shall include a description of the scientific feasibility and rationale for the request. For guidance petitioned under this subparagraph, the Secretary shall, within 2 years of such petition, issue final guidance with respect to that product class.

''(E) REQUIREMENT FOR APPLICATION CONSIDERATION.—The Secretary may not accept an application under this subsection until the Secretary has initiated a proceeding for issuance of guidance with respect to the product class within which the product that is the subject of the application falls. The Secretary may not approve an application under this subsection until the Secretary has completed the proceeding for issuance of guidance with respect to the product class within which the product that is the subject of the application falls.

''(F) REQUIREMENT FOR PRODUCT CLASS-SPECIFIC GUIDANCE.—Product class-specific guidance issued under subparagraph (A) shall include a description of—

''(i) the criteria that the Secretary will use to determine whether a biological product is biosimilar to a reference product in such product class;

''(ii) the criteria, if available, that the Secretary will use to determine whether a biological product meets the standards for interchangeability described in paragraph (4); and

''(iii) the criteria, if available, that the Secretary will use to assess immunogenicity.

''(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 appli-

cation 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 product sponsor shall provide to the applicant a list of relevant patents owned by the ref-

erence 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 product in a treatment indicated in the ap-

plication, 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), (k)(7)(D), 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.

"(6) LIMITATIONS ON ACTIONS FOR DECLARATORY JUDGMENT.—With respect to a patent that is the subject of an explanation under paragraph

(4)(D)(ii), no action for a declaratory judgment that the patent is invalid, unenforceable, or not infringed may be brought under section 2201 of title 28, United States Code, by an applicant prior to the date that is the later of—

"(A) 3 years prior to the date applicable under subsection (k)(7)(A); or

"(B) 120 days after such explanation has been provided.".

(b) 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 (referred 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 sec-

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

SEC. 102. 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.

TITLE II—AMENDMENTS TO PATENT ACT

SEC. 201. AMENDMENTS TO CERTAIN PATENT PROVISIONS.

Section 271(e)(2) of title 35, United States Code is amended—

(1) in subparagraph (A), by striking ''or'' after ''patent'';

(2) in subparagraph (B), by adding ''or'' after the comma at the end; and

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

"(C) a statement under section 351(l)(4)(D)(ii) of the Public Health Service Act,".

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