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110TH CONGRESS
1ST SESSION

H. R. 1956

To amend the Public Health Service Act to provide for the approval of similar biological products, and for other purposes.

IN THE HOUSE OF REPRESENTATIVES

APRIL 19, 2007

Mr. INSLEE (for himself, Mr. GENE GREEN of Texas, and Ms. BALDWIN) introduced the following bill; which was referred to the Committee on Energy and Commerce

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A BILL

To amend the Public Health Service Act to provide for the approval of similar 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 ''Patient Protection and Innovative Biologic Medicines Act of 2007''.

SEC. 2. APPROVAL OF SIMILAR BIOLOGICAL PRODUCTS.

(a) IN GENERAL.—Section 351 of the Public Health Service Act (42 U.S.C. 262) is amended—

(1) in subsection (j), by striking ''under subsection (a)'' and inserting ''under subsection (a) or (k)''; and

(2) by adding at the end the following:

''(k) SIMILAR BIOLOGICAL PRODUCTS.—

''(1) APPLICATION.—

''(A) SUBMISSION.—Any person may submit an application under this subsection for approval of a biologics license for a biological product (in this section referred to as the 'similar biological product') that is claimed to be similar to a qualified biological product (in this subsection referred to as the 'reference product').

''(B) DEFINITION.—In this subsection, the term 'qualified biological product' means a biological product that is a biotechnology-derived therapeutic biological product licensed under subsection (a) or a biotechnology-derived therapeutic protein product subject to an approved application that was submitted under section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act.

''(2) REVIEW AND APPROVAL OF SIMILAR BIOLOGICAL PRODUCT APPLICATIONS.—

''(A) REVIEW.—An application submitted under this subsection for a similar biological product shall be reviewed—

''(i) by the division that was responsible for review and approval of the reference product; and

''(ii) in accordance with the procedures for review of biologics license applications established by the Secretary pursuant to subsection (a)(2)(A).

''(B) APPROVAL.—The Secretary shall approve the application submitted under paragraph (1) only if—

''(i) the applicant demonstrates that the similar biological product conforms to the applicable final product-class specific guidance and, on the basis of the data submitted in conformance with such guidance, the Secretary concludes the product is safe, pure, and potent;

''(ii) the facility in which the similar biological product is manufactured, processed, packed, or held meets standards designed to assure that the biological product continues to be safe, pure, and potent; and

"(iii) 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).

"(C) CONDITIONS OF APPROVAL.—The Secretary may approve an application submitted under paragraph (1) for a similar biological product—

"(i) only for indications for which the reference product is approved; and

"(ii) only if, with respect to each such indication, the application conforms to the applicable final product-class specific guidance, and on the basis of non-clinical and clinical data submitted regarding such indication, the Secretary concludes the product is safe, pure, and potent.

"(D) THERAPEUTIC EQUIVALENCE.—The Secretary shall not designate a similar biological product as therapeutically equivalent to the reference product.

"(3) TIME FRAMES FOR APPLICATION AND AUTHORIZATION.—

''(A) SUBMISSION OF APPLICATIONS.—No application for a similar biological product may be submitted under this subsection unless—

''(i) the Secretary has published under paragraph (5) final product-class specific guidance applicable to the reference product; and

''(ii) not less than 12 years have elapsed from the date on which the reference product was approved or licensed.

''(B) EFFECTIVE DATE OF APPROVAL.—Subject to subparagraph (C), approval of an application submitted under paragraph (1) shall not be made effective until at least 14 years have elapsed from the date on which the reference product was approved or licensed.

''(C) SIGNIFICANT CLINICAL BENEFIT.—Approval of an application submitted under paragraph (1) shall not be made effective until at least 15 years have elapsed from the date on which the reference product was approved or licensed if—

''(i) during the 12-year period following the approval or licensing of the reference product, the Secretary approves a

supplement to the new drug or biologics license application for the reference product that seeks approval to market the reference product for a new indication; and

''(ii) in the opinion of the Secretary, the new indication provides a significant clinical benefit in comparison with existing therapies.

''(D) EXCLUSIVE APPROVAL PATHWAY.—The Secretary may not approve, under any other provision of law, a product that is claimed to be similar to or the same as a reference product.

''(4) REQUESTS FOR ISSUANCE OF PRODUCT-CLASS SPECIFIC GUIDANCE.—

''(A) IN GENERAL.—Any person may submit a request to the Secretary for the issuance of product-class specific guidance applicable to a qualified biological product and its class.

''(B) PRIORITY.—The Secretary—

''(i) in prioritizing among requests under this paragraph for guidance, shall consider likely market entry dates of similar biological products and the amount of time that will be needed to prepare the re-

quested product-class specific guidance; and

''(ii) may summarily reject frivolous or unsupported requests.

''(C) ISSUANCE OF GUIDANCE.—In response to a request under this paragraph, the Secretary shall—

''(i) publish in the Federal Register a concept paper setting forth the specific questions to be addressed in product-class specific guidance and invite comments on the concept paper from any interested persons;

''(ii) accept comments on the concept paper for not less than 4 months;

''(iii) consider the public comments on the concept paper;

''(iv) publish in the Federal Register proposed product-class specific guidance and invite comments on the proposed guidance from any interested persons;

''(v) accept comments on the proposed guidance for not less than 6 months;

''(vi) obtain the advice of the Similar Biological Products Advisory Committee with respect to the proposed guidance; and

''(vii) except as provided in subparagraph (D), not later than 24 months after receipt of the initial request, publish in the Federal Register final product-class specific guidance or a determination that, given the current state of scientific and technical knowledge, it is not possible to issue product-class specific guidance setting forth data that will ensure the safety, purity, and potency of similar biological products to be covered by the guidance.

''(D) CONSOLIDATION OF REQUESTS.—The Secretary may consolidate requests submitted under this paragraph that refer to closely related products or product classes. If the Secretary chooses to consolidate such requests, the Secretary shall publish final product-class specific guidance or a determination described in subparagraph (C)(vii) not later than 30 months after receipt of the first request for guidance for any product in the class.

''(5) PRODUCT-CLASS SPECIFIC GUIDANCE.—

''(A) IN GENERAL.—Guidance published under paragraph (4) shall describe the data and information that will be required in an application submitted under paragraph (1).

''(B) REQUIRED ELEMENTS.—At a minimum, guidance published under paragraph (4) shall require—

''(i) data demonstrating the consistency and robustness of the manufacturing process for an active ingredient of the similar biological product and the finished formulation of the similar biological product;

''(ii) data demonstrating the stability, compatibility (such as with excipients), and biological and physicochemical integrity of the active ingredient of the similar biological product;

''(iii) data from physical, chemical, and biological assays fully characterizing the similar biological product, in comparison with the reference product, at both the active ingredient and finished product levels;

''(iv) data from comparative nonclinical studies demonstrating that the similar biological product and the reference product have similar profiles in terms of pharmacokinetics, pharmacodynamics, toxicity, immunogenicity, and other relevant factors;

''(v) data from comparative clinical trials demonstrating that the similar biological product and the reference product have similar profiles in terms of safety, purity, and potency, including pharmacokinetic studies, pharmacodynamic studies, and trials of sufficient size and duration to demonstrate that the products are similar in their safety (in terms of nature, seriousness, and frequency of adverse reactions), purity, and potency profiles; and

''(vi) a plan for postmarketing safety monitoring (in addition to ordinary pharmacovigilance), including with respect to clinical trials; antibody testing and, as appropriate, other tests to investigate immunogenicity; patient registries; and other surveillance measures to monitor the

clinical safety and risk-benefit balance of the similar biological product.

''(6) REVISIONS TO GUIDANCE.—If a new condition of use is approved for a reference product after the latest publication of the final product-class specific guidance applicable to such product, the Secretary shall promptly update and republish the guidance in accordance with paragraphs (4) and (5) (irrespective of whether a request for such revision has been received under paragraph (4)(A)) to address the data and information that will be required in an application under this subsection for approval of the new condition of use. The requirements of paragraph (2)(C) shall apply if the new condition of use is a new indication.

''(7) SIMILAR BIOLOGICAL PRODUCTS ADVISORY COMMITTEE.—

''(A) ESTABLISHMENT.—The Secretary shall establish a Similar Biological Products Advisory Committee (in this paragraph referred to as the 'Committee').

''(B) DUTIES.—The Committee shall—

''(i) provide expert scientific advice and recommendations to the Secretary re-

garding the development and approval of similar biological products; and

''(ii) in formulating such advice and recommendations, provide interested persons with a reasonable opportunity to make written and oral presentations.

''(C) MEMBERSHIP.—

''(i) QUALIFICATIONS.—The Secretary shall appoint to serve on the Committee individuals with expertise on therapeutic biological products, including manufacturing, safety, effectiveness, and other relevant matters. The Secretary shall ensure that the Committee consists of members with adequately diversified expertise and practical experience in such fields as clinical medicine, biological and physical sciences, pharmacoepidemiology and postmarket safety surveillance, and related professions.

''(ii) NOMINATIONS.—In appointing members of the Committee, the Secretary shall provide an opportunity for scientific, industry, and consumer organizations and the public to nominate such members.

"(iii) NONVOTING MEMBERS.—The Committee shall include, as nonvoting members, representatives of patient organizations, manufacturers of innovative biological products, and manufacturers of similar biological products.

"(iv) SUPPLEMENTAL MEMBERSHIP.—For the purpose of developing product-class specific guidance under paragraphs (4) and (5), the Secretary may supplement the membership of the Committee, or arrange for advice from another advisory committee, in order to obtain the advice of individuals with special expertise relating to any product under review.

"(l) PROPER NAME.—For purposes of this section:

"(1) BIOTECHNOLOGY-DERIVED THERAPEUTIC PROTEINS.—

"(A) IN GENERAL.—Subject to subparagraph (D), the term 'proper name', with respect to a biotechnology-derived therapeutic protein, means—

"(i) the name adopted for such protein by the United States Adopted Names

Council if such name is a unique USAN; or

"(ii) if the biotechnology-derived therapeutic protein lacks a unique USAN, an official name designated pursuant to subparagraph (C).

"(B) UNIQUE USAN.—The term 'unique USAN', with respect to a biotechnology-derived therapeutic protein, means a name adopted for such protein by the United States Adopted Names Council that has not been adopted for any protein manufactured by a different person.

"(C) DESIGNATION.—The Secretary shall designate an official name for any biotechnology-derived therapeutic protein that lacks a unique USAN. Any official name designated under this subparagraph shall be the only official name of that protein used in any official compendium published after such name has been designated. In no event, however, shall the Secretary designate an official name so as to infringe a valid trademark. Any designation under this subparagraph shall be made by rule in accordance with section 553 of title 5, United States Code.

"(D) EXCEPTION.—The term 'proper name', with respect to a biotechnology-derived therapeutic protein that was licensed by the Secretary prior to the effective date of the Patient Protection and Innovative Biologic Medicines Act of 2007, means the name adopted for such protein by the United States Adopted Names Council, irrespective of whether such name is a unique USAN.

"(2) OTHER BIOLOGICAL PRODUCTS.—The term 'proper name', with respect to a biological product that is not a biotechnology-derived therapeutic protein, means—

"(A) the official name designated by the Secretary for such biological product pursuant to section 508 of the Federal Food, Drug, and Cosmetic Act;

"(B) if there is no such official name and such biological product is an article recognized in an official compendium, the official title thereof in such compendium; or

"(C) if neither subparagraph (A) nor subparagraph (B) applies, the common or usual name, if any, of such biological product.".

(b) CONFIDENTIALITY.—Subsection (j) of section 351 of the Public Health Service Act (42 U.S.C. 262), as amended by subsection (a)(1), is further amended by adding at the end the following: ''The Secretary shall maintain the confidentiality of information submitted under this section for a biological product to the same extent and in the same manner as the Secretary maintains the confidentiality of information submitted under section 505 of the Federal Food, Drug, and Cosmetic Act for a drug.''.

SEC. 3. AMENDMENTS TO FEDERAL FOOD, DRUG, AND COSMETIC ACT.

(a) LABELING.—Section 502 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 352) is amended by adding at the end the following:

''(y) If it is a biotechnology-derived therapeutic protein, it was licensed under section 351 of the Public Health Service Act prior to the effective date of the Patient Protection and Innovative Biologic Medicines Act of 2007, it lacks a unique USAN, and its labeling fails to bear (i) its proper name (as defined in section 351(l) of the Public Health Service Act); (ii) its brand name or phrasing, approved by the Secretary, that adequately distinguishes it from other approved biotechnology-derived therapeutic proteins with the same proper name; and (iii)

the following warning: 'Any change in [insert the proper name of the product], including a change in manufacturer, should be made cautiously and only if authorized by and supervised by the prescribing health care professional.'. The requirement in the preceding sentence regarding the inclusion of a warning applies beginning on the date that is 180 days after the date of the enactment of the Patient Protection and Innovative Biologic Medicines Act of 2007.

''(z) If it is a biotechnology-derived therapeutic protein not subject to paragraph (y), and its labeling fails to include (i) its proper name (as defined in section 351(l) of the Public Health Service Act); and (ii) the following warning: 'This product shall not be dispensed in substitution for another biological product that was prescribed to be dispensed, unless such substitution was expressly authorized by and is supervised by the prescribing health care professional.'. In the case of such a protein that is a similar biological product licensed under section 351(k) of the Public Health Service Act, the warning required by the preceding sentence shall read as follows: 'This product shall not be dispensed in substitution for another biological product that was prescribed to be dispensed including [insert the proprietary name and proper name of the reference product].' ''.

(b) DISPENSING.—Section 503(b) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 353(b)) is amended by adding at the end the following:

''(6) A drug that is subject to paragraph (1) and is a biotechnology-derived therapeutic protein licensed under section 351 of the Public Health Service Act shall not be dispensed unless the prescription specifies the drug's proprietary name or, if the drug lacks a proprietary name, the drug's proper name (as defined in section 351(l) of such Act). The act of dispensing a drug contrary to the preceding sentence shall be deemed to be an act which results in the drug being misbranded while held for sale.''.

SEC. 4. REPORTS TO CONGRESS.

(a) EXTENSION OF APPROVAL PATHWAY TO OTHER PRODUCTS.—Not later than 2 years after the date of the enactment of this Act, and every 2 years thereafter, the Secretary of Health and Human Services shall submit a report to the Congress making recommendations on whether it is feasible, in the current state of scientific and technical knowledge, to approve applications under subsection 351(k) of the Public Health Service Act, as added by section 2 of this Act, for biological products that are claimed to be similar to vaccines, blood or plasma products or their derivatives, gene therapy, cell processing, naturally derived therapeutic proteins, or other biological prod-

ucts that do not contain biotechnology-derived therapeutic proteins as their active ingredients.

(b) THERAPEUTIC EQUIVALENCE DETERMINATIONS.—Not later than 2 years after the date of the enactment of this Act, and every 2 years thereafter, the Secretary of Health and Human Services shall submit a report to the Congress making recommendations on—

(1) whether it is feasible, in the current state of scientific and technical knowledge, to make therapeutic equivalence determinations for similar biological products approved under section 351(k) of the Public Health Service Act, as added by section 2 of this Act; and

(2) if so, the statutory criteria that should govern such determinations.

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