Section 351(k) of the Public Health Service Act.

[…]

(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~~*(A) IN GENERAL.—An application submitted under this subsection shall include information* demonstrating that—

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

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

(II) (bb) an assessment of toxicity (which may rely on, or consist of, a study or studies described in item (aa) or (cc)); and

(III) (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 licensed and intended to be used and for which licensure is sought for the biological product;

(ii)~~(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) ~~(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) ~~(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) ~~(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)~~(ii)~~ Determination by secretary.—The Secretary may determine, in the Secretary's discretion, that an element described in ~~clause (i)(I)~~ subparagraph (A)(i) is unnecessary in an application submitted under this subsection.

(C)~~(iii)~~ Additional information.—An application submitted under this subsection—

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

(ii) ~~(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; and

(iii) ~~(III)~~ may include information to show that the conditions of use prescribed, recommended, or suggested in the labeling proposed for the biological product have been previously approved for the reference product.

~~(B) Interchangeability.—An application (or a supplement to an application) submitted 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 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—~~

~~(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.~~

INTERCHANGEABILITY.—

(A) IN GENERAL.—A biological product licensed under this subsection shall be deemed to be interchangeable with the reference product.

(B) CONGRESSIONAL BRIEFING PRIOR TO CERTAIN STUDY REQUIREMENTS.—The Secretary may require the sponsor of an application submitted under this section to conduct a study to evaluate the risk, in terms of safety, purity, or potency, of alternating or switching between the use of the biological product that is the subject of the application and the reference product, if, before requiring such a study, the Secretary first holds a private briefing with the chair and ranking member of the Committee on Health, Education, Labor, and Pensions of the Senate and the chair and the ranking member of the Committee on Energy and Commerce of the House of Representatives, to explain why such a study is necessary for the biological product, what information the Secretary expects such a study to reveal, what alternatives to such study have been considered, and why those alternatives are not sufficient.

(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).

~~(6) Exclusivity for first interchangeable biological product.—The Secretary shall not make approval as an interchangeable biological product effective with respect to an application submitted under this subsection that relies on the same reference product for which a prior biological product has received a determination of interchangeability 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)(6) 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)(6) 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)(6) 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)(6).~~

~~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, and the term "first interchangeable biosimilar biological product" means any interchangeable biosimilar biological product that is approved on the first day on which such a product is approved as interchangeable with the reference product.~~

(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.

(D) Deemed licenses.—

(i) No additional exclusivity through deeming.—An approved application that is deemed to be a license for a biological product under this section pursuant to section 7002(e)(4) of the Biologics Price Competition and Innovation Act of 2009 shall not be treated as having been first licensed under subsection (a) for purposes of subparagraphs (A) and (B).

(ii) Application of limitations on exclusivity.—Subparagraph (C) shall apply with respect to a reference product referred to in such subparagraph that was the subject of an approved application that was deemed to be a license pursuant to section 7002(e)(4) of the Biologics Price Competition and Innovation Act of

2009.

(iii) Applicability.—The exclusivity periods described in section 527, section 505A(b)(1)(A)(ii), and section 505A(c)(1)(A)(ii) of the Federal Food, Drug, and Cosmetic Act shall continue to apply to a biological product after an approved application for the biological product is deemed to be a license for the biological product under subsection (a) pursuant to section 7002(e)(4) of the Biologics Price Competition and Innovation Act of 2009.

(8) 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~~ *description of 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~~ *class.*

~~(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.

(9) Public listing.—

(A) In general.—

(i) Initial publication.—Not later than 180 days after the date of enactment of this paragraph, the Secretary shall publish and make available to the public in a searchable, electronic format—

(I) a list of each biological product, by nonproprietary name (proper name), for which, as of such date of enactment, a biologics license under subsection (a) or this subsection is in effect, or that, as of such date of enactment, is deemed to be licensed under this section pursuant to section 7002(e)(4) of the Biologics Price Competition and Innovation Act of 2009;

(II) the date of licensure of the marketing application and the application number; and

(III) with respect to each biological product described in subclause (I), the licensure status, and, as available, the marketing status.

(ii) Revisions.—Every 30 days after the publication of the first list under clause (i), the Secretary shall revise the list to include each biological product which has been licensed under subsection (a) or this subsection during the 30-day period or deemed licensed under this section pursuant to section 7002(e)(4) of the Biologics Price Competition and Innovation Act of 2009.

(iii) Patent information.—Not later than 30 days after a list of patents under subsection (l)(3)(A), or a supplement to such list under subsection (l)(7), has been provided by the reference product sponsor to the subsection (k) applicant respecting a biological product included on the list published under this subparagraph, the reference product sponsor shall provide such list of patents (or supplement thereto) and their corresponding expiry dates to the Secretary, and the Secretary shall, in revisions made under clause (ii), include such information for such biological product. Within 30 days of providing any subsequent or supplemental list of patents to any subsequent subsection (k) applicant under subsection (l)(3)(A) or (l)(7), the reference product sponsor shall update the information provided to the Secretary under this clause with any additional patents from such subsequent or supplemental list and their corresponding expiry dates.

(iv) Listing of exclusivities.—For each biological product included on the list published under this subparagraph, the Secretary shall specify each exclusivity period under paragraph (6) or paragraph (7) for which the Secretary has determined such biological product to be eligible and that has not concluded.

(B) Revocation or suspension of license.—If the license of a biological product is determined by the Secretary to have been revoked or suspended for safety, purity, or

potency reasons, it may not be published in the list under subparagraph (A). If such revocation or suspension occurred after inclusion of such biological product in the list published under subparagraph (A), the reference product sponsor shall notify the Secretary that—

(i) the biological product shall be immediately removed from such list for the same period as the revocation or suspension; and

(ii) a notice of the removal shall be published in the Federal Register.

Section 351(i) of the Public Health Service Act.

[…]

(i) In this section:

(1) The term "biological product" means a virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, protein, or analogous product, or arsphenamine or derivative of arsphenamine (or any other trivalent organic arsenic compound), applicable to the prevention, treatment, or cure of a disease or condition of human beings.

(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)~~ licensed under subsection (k), 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).

SEC. 352A. [263-1] of the Public Health Service Act - EDUCATION ON BIOLOGICAL PRODUCTS.

(a) Internet Website.—

(1) In general.—The Secretary may maintain and operate an internet website to provide educational materials for health care providers, patients, and caregivers, regarding the meaning of the terms, and the standards for review and licensing of, biological products, including biosimilar biological products ~~and interchangeable biosimilar biological products~~.

(2) Content.—Educational materials provided under paragraph (1) may include—

(A) explanations of key statutory and regulatory terms, including "biosimilar" and "interchangeable", and clarification regarding the use of interchangeable biosimilar biological products;

(B) information related to development programs for biological products, including biosimilar biological products ~~and interchangeable biosimilar biological products~~ and relevant clinical considerations for prescribers, which may include, as appropriate and applicable, information related to the comparability of such biological products;

(C) an explanation of the process for reporting adverse events for biological products, including biosimilar biological products ~~and interchangeable biosimilar biological products~~; and

(D) an explanation of the relationship between biosimilar biological products ~~and interchangeable biosimilar biological products~~ licensed under section 351(k) and reference products (as defined in section 351(i)), including the standards for review and licensing of each such type of biological product.

(3) Format.—The educational materials provided under paragraph (1) may be—

(A) in formats such as webinars, continuing education modules, videos, fact sheets, infographics, stakeholder toolkits, or other formats as appropriate and applicable; and

(B) tailored for the unique needs of health care providers, patients, caregivers, and other audiences, as the Secretary determines appropriate.

(4) Other information.—In addition to the information described in paragraph (2), the Secretary shall continue to publish—

(A) the action package of each biological product licensed under subsection (a) or (k) of section 351; or

(B) the summary review of each biological product licensed under subsection (a) or (k) of section 351.

(5) Confidential and trade secret information.—This subsection does not authorize the disclosure of any trade secret, confidential commercial or financial information, or other matter described in section 552(b) of title 5.

(b) Continuing Education.—The Secretary shall advance education and awareness among health care providers regarding biological products, including biosimilar biological products ~~and interchangeable biosimilar biological products~~, as appropriate, including by developing or improving continuing education programs that advance the education of such providers on the

prescribing of, and relevant clinical considerations with respect to, biological products, including biosimilar biological products ~~and interchangeable biosimilar biological products~~.

Section 744G(14) of the FFD&CA

[…]

(14) The term "supplement" means a request to the Secretary to approve a change in a biosimilar biological product application which has been approved~~, including a supplement requesting that the Secretary determine that the biosimilar biological product meets the standards for interchangeability described in section 351(k)(4) of the Public Health Service Act.~~

Section 505B of the FFD&CA

[…]

~~(l) New Active Ingredient.—~~

~~(1) Non-interchangeable biosimilar biological product.—A biological product that is biosimilar to a reference product under section 351 of the Public Health Service Act, and that the Secretary has not determined to meet the standards described in subsection (k)(4) of such section for interchangeability with the reference product, shall be considered to have a new active ingredient under this section.~~

~~(2) Interchangeable biosimilar biological product.—A biological product that is interchangeable with a reference product under section 351 of the Public Health Service Act shall not be considered to have a new active ingredient under this section.~~

(l) BIOSIMILAR BIOLOGICAL PRODUCTS.—A biological product for which an application is submitted under section 351(k) of the Public Health Service Act shall be considered to have a new active ingredient for purposes of this section, except that a pediatric assessment shall not be required for a claimed indication in a relevant pediatric population if the assessment would involve—

(1) a condition of use that has not been previously approved for the reference product; or

(2) a dosage form, strength, or route of administration that differs from that of the reference product.