I

114TH CONGRESS
1ST SESSION

H. R. 1576

To require a study by the Government Accountability Office (GAO) to assess the Food and Drug Administration's current regulatory pathway for reviewing generic versions of nonbiologic complex drug products, and for other purposes.

IN THE HOUSE OF REPRESENTATIVES

MARCH 24, 2015

Mr. BURGESS (for himself, Mr. BUTTERFIELD, Mr. ASHFORD, and Mr. BILIRAKIS) introduced the following bill; which was referred to the Committee on Energy and Commerce

---

A BILL

To require a study by the Government Accountability Office (GAO) to assess the Food and Drug Administration's current regulatory pathway for reviewing generic versions of nonbiologic complex drug 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 ''Generic Complex Drugs Safety and Effectiveness for Patients Act of 2015''.

SEC. 2. GAO STUDY OF SCIENTIFIC ISSUES REGARDING THE CURRENT REGULATORY PATHWAY FOR REVIEWING GENERIC VERSIONS OF CERTAIN COMPLEX DRUG PRODUCTS.

(a) STUDY BY GAO.—The Comptroller General of the United States shall conduct a study to determine the following:

(1) With respect to nonbiologic complex drug products that have not been fully characterized (as defined in subsection (e)(1)), whether the listing of such drugs as reference products in generic drug applications presents unique challenges in meeting approval standards that are significantly different than the challenges presented by generic drug applications that list small-molecule reference products.

(2) With respect to biological products that are within the scope of the exception under section 7002(e)(2) of Public Law 111–148 (relating to temporary authority for the approval of biological products under section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355)), whether the listing of such biological products as reference products in generic drug applications presents unique challenges in meeting approval standards that are significantly different than the challenges presented

by generic drug applications that list small-molecule reference products.

(3) If the answer to the question under paragraph (1) or (2) is that significantly different challenges are presented for patients when reference products are nonbiologic complex drug products that have not been fully characterized or when reference products are biological products that are within the scope of the exception under section 7002(e)(2) of Public Law 111–148:

(A) What degree of characterization of the proposed generic version and the reference product should be required in order to determine the safety and effectiveness of the generic version.

(B) What degree of similarity should be required to deem that the active ingredient of the proposed generic version is the same as the active ingredient of the reference product.

(C) What types of evidence should be required to demonstrate that the proposed generic version is bioequivalent to the reference product.

(D) What requirements should be established with respect to the comparability of the

manufacturing process for the proposed generic version and the manufacturing process for the reference product.

(E) Whether and to what extent clinical evidence is needed to demonstrate that there is no difference in immunogenicity between the proposed generic version and the reference product.

(F) Whether and to what extent other clinical evidence is needed to demonstrate that the proposed generic version is as safe and effective for patients as the reference product.

(G) Taking into account the determinations made regarding the issues listed in subparagraphs (A) through (F):

(i) Whether section 505(j) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(j)) should be amended to establish provisions that expressly address the approval of copy versions of nonbiologic complex drug products that have not been fully characterized, provisions that expressly address the approval of copy versions of biological products that are within the scope of the exception under

section 7002(e)(2) of Public Law 111–148, or both.

(ii) Whether section 505(b)(2) of such Act (21 U.S.C. 355(b)(2)) should be so amended.

(iii) Whether such Act should otherwise be so amended.

(iv) Whether section 351 of the Public Health Service Act (42 U.S.C. 262) should be so amended.

(H) Taking into account the determinations made regarding the issues listed in subparagraphs (A) through (F), and taking into consideration all relevant guidances, draft guidances, and other agency policy documents—

(i) whether the Food and Drug Administration should develop and provide to the public a policy document that provides a comprehensive statement of general principles on the evidence that is necessary to obtain the approval of such Administration for proposed generic versions of reference products that are nonbiologic complex drug products that have not been fully characterized or that are biological products; and

(ii) if so, the date by which such Administration could reasonably be expected to issue such comprehensive policy document.

(b) CONSULTATION.—The Comptroller General shall conduct the study under subsection (a) in consultation with—

(1) the Secretary of Health and Human Services, acting through the Commissioner of Food and Drugs; and

(2) appropriate public and private entities, including patient advocacy organizations, professional medical associations, hospital pharmacies, scientists of academic and business organizations, and representatives of the regulated industry.

(c) REQUIRED CONSIDERATION.—In carrying out the study under subsection (a), the Comptroller General shall consider the following:

(1) Published clinical reports of clinically meaningful (including serious) adverse events of patients to—

(A) generic versions of the nonbiologic complex drug products that have not been fully characterized;

(B) generic versions of biological products; and

(C) the reference products.

(2) The specific criteria that have been used by the Secretary to approve generic versions of nonbiologic complex drug products that have not been fully characterized or generic versions of biological products.

(3) The specific criteria specified in guidances, draft guidance, and other documents issued by the Secretary regarding applications under section 351(k) of the Public Health Service Act (42 U.S.C. 262(k)) for the licensing of biosimilar biological products.

(d) OPTIONAL CONSIDERATION.—In carrying out the study under subsection (a), the Comptroller General may under subsection (c) consider the following information from foreign countries:

(1) Reports described in subsection (c)(1) from foreign countries that are listed in clause (i) or (ii) of section 802(b)(1)(A) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 382(b)(1)(A)) or are designated pursuant to section 802(b)(1)(B) of such Act (21 U.S.C. 382(b)(1)(B)).

(2) The guidelines or recommendations of the pharmaceutical regulatory agencies of foreign countries described in paragraph (1) regarding any class of products that such an agency regulates as a biosimilar biological product, but that has been or could be approved as a generic drug in the United States.

(3) Any instance where the Secretary or such foreign regulatory agencies have, after approving a generic version (or a foreign equivalent) of a nonbiologic complex drug product that has not been fully characterized or a generic version (or a foreign equivalent) of a biological product, sought a clinical trial to confirm—

(A) the generic version (or foreign equivalent) is therapeutically equivalent to the reference product (or meets a similar standard, in the case of a foreign regulatory agency); or

(B) the safety and effectiveness of the generic version (or foreign equivalent).

(e) COMPLETION DATE.—Not later than the expiration of the 2-year period beginning on the date of the enactment of this Act, the Comptroller General shall complete the study under subsection (a) and submit a report describing the findings and conclusions of the study to the Secretary, the Committee on Energy and Commerce of the

House of Representatives, and the Committee on Health, Education, Labor, and Pensions of the Senate.

(f) DEFINITIONS.—

(1) COMPLEX DRUG PRODUCT NOT FULLY CHARACTERIZED.—For purposes of this section, the terms ''complex drug product that has not been fully characterized'' and ''complex drug products that have not been fully characterized'', with respect to a nonbiologic drug, means a drug for which—

(A) the active ingredient has molecular diversity;

(B) scientific analytic methodologies are unable to fully identify the molecular structures and physiochemical properties of the active ingredient; and

(C) the nature of the active ingredient is not understood sufficiently to identity—

(i) all the molecular components of the drug that are involved in producing the therapeutic effect; and

(ii) the mechanisms of action that produce such effect.

(2) OTHER DEFINITIONS.—For purposes of this section:

(A) The term ''bioequivalent'', with respect to a generic drug, has the meaning given such term in section 505(j)(8)(B) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(j)(8)(B)).

(B) The term ''generic drug'' or ''generic version'', with respect to the United States, means a drug that is approved under section 505(j) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(j)).

(C) The term ''generic drug application'' means an abbreviated application for the approval of a new drug under section 505(j) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(j)).

(D) The term ''proposed'', with respect to a generic version, means subject to a generic drug application that is pending before the Food and Drug Administration.

(E) The term ''reference product'', with respect to a generic drug, has the meaning given the term ''listed drug'' in section 505(j) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(j)).

(F) The term ''Secretary'' means the Secretary of Health and Human Services.

○