



4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 15

[Docket No. FDA-2018-N-2689]

Facilitating Competition and Innovation in the Biological Products Marketplace; Public Hearing; Request for Comments

AGENCY: Food and Drug Administration, HHS.

ACTION: Notification of public hearing; request for comments.

SUMMARY: The Food and Drug Administration (FDA or the Agency) is announcing a public hearing on FDA's approach to enhancing competition and innovation in the biological products marketplace, including by facilitating greater availability of biosimilar and interchangeable products.

DATES: The public hearing will be held on Tuesday, September 4, 2018, from 9 a.m. to 5 p.m.

The public hearing may be extended or may end early, depending on the level of public participation. Persons seeking to attend or to present at the public hearing must register by Tuesday, August 14, 2018. Section III provides attendance and registration information.

Electronic or written comments will be accepted after the public hearing until Friday, September 21, 2018.

ADDRESSES: The public hearing will be held at the FDA White Oak Campus, 10903 New Hampshire Ave., Bldg. 31 Conference Center, the Great Room (Rm. 1503A), Silver Spring, MD 20993-0002. Entrance for public hearing participants (non-FDA employees) is through Building 1, where routine security check procedures will be performed. For parking and security

information, please refer to

<https://www.fda.gov/AboutFDA/WorkingatFDA/BuildingsandFacilities/WhiteOakCampusInformation/ucm241740.htm>.

You may submit comments as follows. Please note that late, untimely filed comments will not be considered. Electronic comments must be submitted on or before Friday, September 21, 2018. The <https://www.regulations.gov> electronic filing system will accept comments until midnight Eastern Time at the end of Friday, September 21, 2018. Comments received by mail/hand delivery/courier (for written/paper submissions) will be considered timely if they are postmarked or the delivery service acceptance receipt is on or before that date.

Electronic Submissions

Submit electronic comments in the following way:

- Federal eRulemaking Portal: <https://www.regulations.gov>. Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to <https://www.regulations.gov> will be posted to the docket unchanged. Because your comment will be made public, you are solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else's Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on <https://www.regulations.gov>.

- If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see "Written/Paper Submissions" and "Instructions").

Written/Paper Submissions

Submit written/paper submissions as follows:

- Mail/Hand delivery/Courier (for written/paper submissions): Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.
- For written/paper comments submitted to the Dockets Management Staff, FDA will post your comment, as well as any attachments, except for information submitted, marked, and identified as confidential, if submitted as detailed in "Instructions."

Instructions: All submissions received must include the Docket No. FDA-2018-N-2689 for "Facilitating Competition and Innovation in the Biological Products Marketplace; Public Hearing; Request for Comments." Received comments, those filed in a timely manner (see ADDRESSES), will be placed in the docket and, except for those submitted as "Confidential Submissions," publicly viewable at <https://www.regulations.gov> or at the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

- Confidential Submissions--To submit a comment with confidential information that you do not wish to be made publicly available, submit your comments only as a written/paper submission. You should submit two copies total. One copy will include the information you claim to be confidential with a heading or cover note that states "THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION." The Agency will review this copy, including the claimed confidential information, in its

consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on <https://www.regulations.gov>. Submit both copies to the Dockets Management Staff. If you do not wish your name and contact information to be made publicly available, you can provide this information on the cover sheet and not in the body of your comments and you must identify this information as "confidential." Any information marked as "confidential" will not be disclosed except in accordance with 21 CFR 10.20 and other applicable disclosure law. For more information about FDA's posting of comments to public dockets, see 80 FR 56469, September 18, 2015, or access the information at: <https://www.gpo.gov/fdsys/pkg/FR-2015-09-18/pdf/2015-23389.pdf>.

Docket: For access to the docket to read background documents or the electronic and written/paper comments received, go to <https://www.regulations.gov> and insert the docket number, found in brackets in the heading of this document, into the "Search" box and follow the prompts and/or go to the Dockets Management Staff, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: Allison Hoffman, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 1, Rm. 1314, Silver Spring, MD 20993, 301-796-9203, OMPTFeedback@fda.hhs.gov.

SUPPLEMENTARY INFORMATION:

I. Background

The Biologics Price Competition and Innovation Act of 2009 (BPCI Act) amended the Public Health Service Act (PHS Act) and other statutes to create an abbreviated licensure

pathway for biological products shown to be biosimilar to, or interchangeable with, an FDA-licensed biological reference product. The BPCI Act was intended to balance innovation and consumer interests. The abbreviated licensure pathway, in section 351(k) of the PHS Act, allows an applicant (a "351(k) applicant") to rely, in part, on FDA's previous determination of safety and effectiveness for the reference product for approval. The BPCI Act provides, among other things, exclusivity periods for certain biological products licensed in "stand alone" applications under section 351(a) of the PHS Act.

As the marketplace of biological products continues to expand and evolve, FDA expects that increased availability of biosimilars and interchangeable products will result in more competition and create savings for patients and the healthcare system. At the same time, we recognize that there are challenges to the rapid growth of this marketplace. For instance, although FDA has approved 11 marketing applications for biosimilars as of July 1, 2018, FDA is aware that the majority of biosimilars licensed by FDA have not yet been marketed and are not available to patients.

Although such delays in the market entry of an approved biosimilar are outside FDA's control, we remain focused on FDA's critical role in increasing the availability of biosimilars and interchangeable products. Recognizing that this is a crucial time in the emergence of the marketplace of biosimilar and interchangeable products, FDA recently developed a Biosimilars Action Plan. This Plan focuses on four key areas: (1) improving the efficiency of the biosimilar and interchangeable product development and approval process; (2) maximizing scientific and regulatory clarity for the biosimilar product development community; (3) developing effective communications to improve understanding of biosimilars among patients, clinicians, and payors;

and (4) supporting market competition by reducing gaming of FDA requirements or other attempts to unfairly delay competition.

FDA's Biosimilars Action Plan builds on the Agency's substantial progress, to date, implementing the approval pathway for biosimilar and interchangeable products. For example, FDA has issued guidance for industry on numerous scientific and regulatory issues related to the development of proposed biosimilar and interchangeable products. FDA also created the Biosimilar Product Development (BPD) Program to facilitate the rapid development of biosimilar and interchangeable products. Through enrollment in this program, FDA provides detailed, product-specific advice to manufacturers. As of July 1, 2018, 68 programs were enrolled in the BPD Program and FDA had received meeting requests to discuss the development of biosimilars for 31 different reference products.

FDA has also prioritized its efforts to provide useful information about licensed biological products to the public. FDA publishes the *Purple Book: Lists of Licensed Biological Products with Reference Product Exclusivity and Biosimilarity or Interchangeability Evaluations*¹ to provide information on licensed biological products, including information on exclusivity for reference products and on whether a product has been demonstrated to be biosimilar to, or interchangeable with, a reference product. Another FDA priority is the development of educational materials for patients, healthcare providers, and other stakeholders to increase knowledge about biological products, including biosimilar and interchangeable products. For example, FDA launched an educational campaign in October 2017 to promote understanding by healthcare providers of biosimilar and interchangeable products and how these

¹<https://www.fda.gov/drugs/developmentapprovalprocess/howdrugsaredevelopedandapproved/approvalapplications/therapeuticbiologicapplications/biosimilars/ucm411418.htm>

products can help patients (see,

<https://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/TherapeuticBiologicApplications/Biosimilars/ucm580435.htm>).

As FDA continues working to implement the BPCI Act, FDA welcomes input from the public on how the Agency can enhance its efforts to increase access by patients to state-of-the-art, lifesaving treatment options by encouraging innovation and competition in the biological products marketplace. FDA will hold a public hearing on September 4, 2018, from 9 a.m. to 5 p.m., to provide an opportunity for all interested stakeholders to submit comments.

The format of the hearing involves presentations from the public. The Agency will not be inviting specific presenters; rather, with this document, FDA is soliciting presentations from interested stakeholders. FDA also invites interested persons to submit written comments to the docket on the topics described in section II.

II. Purpose and Scope of the Public Hearing

FDA is soliciting input from the public on how to facilitate greater availability of biosimilar and interchangeable products while retaining the balance between competition and innovation that Congress intended to achieve under the BPCI Act. FDA is holding a public hearing to receive information and comments from a broad group of stakeholders, including patients, researchers, healthcare providers, manufacturers, interested industry, professional organizations, and the public. The Agency has determined that a public hearing is the most appropriate way to ensure public engagement.

FDA welcomes any relevant information that stakeholders wish to share. FDA is particularly interested in stakeholder input on how the Agency can achieve the following goals:

- Facilitate the efficient development of biosimilar and interchangeable products using state-of-the-art science;
- Develop information resources, as well as scientific or regulatory tools, to streamline the development of biosimilar and interchangeable products;
- Enhance the efficiency of FDA review of marketing applications for biosimilar and interchangeable products;
- Provide additional scientific or regulatory clarity regarding FDA's regulation of biological products, including FDA's review and approval of marketing applications for biological products;
- Increase healthcare provider, patient, and payor understanding of biological products, including biosimilar and interchangeable products; and
- Support market competition by addressing attempts to game FDA requirements or otherwise delay market entry of competing biological products.

FDA is also interested in stakeholder input on the following questions about additional steps FDA can take, within its statutory authority, related to the Agency's regulation of biological products:

1. FDA is aware that many of the biosimilar products that have been licensed by FDA are not yet marketed and available to patients. What can FDA do to help biosimilars and interchangeable products reach patients more quickly after these products are licensed?
2. FDA uses the Purple Book to provide information about biological products licensed under section 351 of the PHS Act. What additional information or features could be

- incorporated into the Purple Book to make it more useful to stakeholders, including patients, healthcare providers, pharmacists, and manufacturers?
3. FDA expects that the number of licensed biosimilar and interchangeable products will continue to increase in the coming years. In many, if not most, cases, FDA anticipates that multiple products will be licensed as biosimilar to, or interchangeable with, a given reference product. What additional steps can FDA take to facilitate the evolution of the biosimilar and interchangeable product marketplace? What can FDA do to ensure that confidence in these products among patients, healthcare providers, pharmacists, and other stakeholders will continue to grow?
 4. Extensive analytical characterization of the proposed biosimilar product and the reference product serves as the foundation for a demonstration of biosimilarity. FDA recognizes that obtaining and testing multiple lots of the reference product adds to the costs of developing a biosimilar product. What can FDA do to help reduce development costs arising from analytical studies of the reference product without compromising FDA's robust scientific standards for licensure of products under section 351(k) of the PHS Act? FDA is particularly interested in stakeholder comments on (1) the number of lots of each product (the proposed biosimilar product and the reference product) that should be used in analytical studies submitted to support licensure of a proposed biosimilar product; and (2) how a 351(k) applicant should account for and evaluate any observed variability in analytical attributes among lots of the reference product or the proposed biosimilar product.
 5. A 351(k) applicant may, with adequate scientific justification, use a non-U.S.-licensed comparator product in certain studies submitted to support licensure of a

- proposed biosimilar product. What additional steps can FDA take to facilitate multinational development programs that may include non-U.S.-licensed comparators, to help support development of biosimilar products?
6. FDA expects continued innovation in the biological product marketplace, including innovation during the lifecycle of reference products licensed under section 351(a) of the PHS Act. What can FDA do to ensure that product changes during the lifecycle of reference products (e.g. changes in product presentation) are adequately incentivized without inappropriately deterring competition from biosimilar and interchangeable products, with the overall goal of balancing of innovation and competition?
 7. Patents or exclusivity may protect one or more conditions of use (e.g. indications) of the reference product. As a result, 351(k) applicants may seek licensure of the proposed biosimilar product for fewer than all of the conditions of use for which the reference product is licensed. Once a condition of use is no longer protected by patents or exclusivity, FDA anticipates that 351(k) applicants often will seek licensure of their product for this condition of use. What challenges do 351(k) applicants face in this context and what should FDA do to achieve the appropriate balance between innovation and competition when one or more conditions of use of the reference product are protected by exclusivity or patents?
 8. The scope of exclusivity under section 351(k)(7) of the PHS Act may also affect biological product innovation and market entry of biosimilars. Accordingly, FDA seeks comment on the potential application of "umbrella exclusivity" under section 351(k)(7). If umbrella exclusivity were to apply in this context, a biological product

- that would not be eligible for a new period of exclusivity under section 351(k)(7)(C) would nevertheless be protected for the duration of the exclusivity period for a previously approved reference product. See, for example, 54 FR 28872 at 28897 (July 10, 1989) for an explanation of how umbrella exclusivity functions under the Hatch-Waxman scheme, a related and potentially instructive context (available at: <https://cdn.loc.gov/service/ll/fedreg/fr054/fr054130/fr054130.pdf>). Thus, umbrella exclusivity could help shield certain biological products that would otherwise not be eligible for their own period of exclusivity under section 351(k)(7)(C) from biosimilar competition. What considerations support recognition of umbrella exclusivity under section 351(k)(7), and what considerations disfavor recognizing umbrella exclusivity? How would umbrella exclusivity promote biological product innovation, and what effect would it have on market entry of biosimilars? What is the relevance and significance, if any, of the patent scheme in considering this issue?
9. What other challenges have the potential to disrupt the balance between innovation and competition in the biological product marketplace and how can FDA or other stakeholders address these challenges?

III. Participating in the Public Hearing

Registration and Requests for Oral Presentations: The FDA Conference Center at the White Oak location is a Federal facility with security procedures and limited seating. Attendance will be free and on a first-come, first-served basis. If you wish to attend (either in person or by webcast (see *Streaming Webcast of the Public Hearing*)) and/or present at the hearing, please register for the hearing and, if appropriate, request an oral presentation or participation in the open public hearing by sending an email to OMPTfeedback@fda.hhs.gov by

Tuesday, August 14, 2018. Requests for participation in the open public hearing are accepted until 9 a.m. on Tuesday September 4, 2018, and will be accepted as long as time allows. The email should contain complete contact information for each attendee (name, title, degree(s), affiliation, address, email address, and telephone number). For those wishing to present at the hearing, the email should also include a presentation title. Those without email access can register by contacting Allison Hoffman at 301-796-9203 by Tuesday, August 14, 2018 (see FOR FURTHER INFORMATION CONTACT). An agenda for the hearing and any other background materials will be made available 5 days before the hearing at <https://www.fda.gov/NewsEvents/MeetingsConferencesWorkshops/UCM610692.htm>.

FDA will try to accommodate all persons who wish to make a presentation. Individuals wishing to present should identify the number of the specific question, or questions, they wish to address. This will help FDA organize the presentations. Individuals and organizations with common interests should consolidate or coordinate their presentations and request time for a joint presentation. FDA will notify registered presenters of their scheduled presentation times. The time allotted for each presenter will depend on the number of individuals who wish to speak. Presenters are encouraged to submit an electronic copy of their presentation (PowerPoint or PDF) to OMPTfeedback@fda.hhs.gov on or before Thursday, August 16, 2018. Those who are not giving electronic presentations are encouraged to submit a single slide (PowerPoint or PDF) with their name, affiliation, and topic. Persons registered to make either an oral presentation or participate as part of the open public hearing are encouraged to arrive at the hearing room early and check in at the onsite registration table to confirm their designated presentation time. An agenda for the hearing and any other background materials will be made available 5 days before

the hearing at

<https://www.fda.gov/NewsEvents/MeetingsConferencesWorkshops/ucm580561.htm>.

If you need special accommodations because of a disability, please contact OMPTFeedback@fda.hhs.gov (see FOR FURTHER INFORMATION CONTACT) no later than Friday, August 17, 2018, at 12 noon Eastern Time.

Streaming Webcast of the Public Hearing: For those unable to attend in person, FDA will provide a live webcast of the hearing. To join the hearing via the webcast, please go to <https://collaboration.fda.gov/biosimilarpart15>.

Transcripts: Please be advised that as soon as a transcript is available, it will be accessible at <https://www.regulations.gov>. It may be viewed at the Dockets Management Staff (see ADDRESSES).

IV. Notification of Hearing Under 21 CFR Part 15

The Commissioner of Food and Drugs is announcing that the public hearing will be held in accordance with part 15 (21 CFR part 15). The hearing will be conducted by a presiding officer, who will be accompanied by FDA senior management from the Office of the Commissioner, the Center for Drug Evaluation and Research, and the Center for Biologics Evaluation and Research. Under § 15.30(f) (21 CFR 15.30(f)), the hearing is informal and the rules of evidence do not apply. No participant may interrupt the presentation of another participant. Only the presiding officer and panel members can pose questions; they can question any person during or at the conclusion of each presentation. Public hearings under part 15 are subject to FDA's policy and procedures for electronic media coverage of FDA's public administrative proceedings (21 CFR part 10, subpart C). Under 21 CFR 10.205, representatives of the media may be permitted, subject to certain limitations, to videotape, film, or otherwise

record FDA's public administrative proceedings, including presentations by participants. The hearing will be transcribed as stipulated in § 15.30(b) (see *Transcripts*). To the extent that the conditions for the hearing, as described in this notification, conflict with any provisions set out in part 15, this notification acts as a waiver of those provisions as specified in § 15.30(h).

Dated: July 19, 2018.

Leslie Kux,

Associate Commissioner for Policy.

[FR Doc. 2018-15859 Filed: 7/24/2018 8:45 am; Publication Date: 7/25/2018]