Biosimilar and Interchangeable Biosimilar Products: Considerations for Container Closure Systems and Device Constituent Parts
Guidance for Industry

DRAFT GUIDANCE

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U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

July 2026
Biosimilars

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Biosimilar and Interchangeable Biosimilar Products: Considerations for Container Closure Systems and Device Constituent Parts Guidance for Industry[1]

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA staff responsible for this guidance as listed on the title page.

I. INTRODUCTION

This guidance describes the Agency's recommendations related to the presentation(s) of proposed therapeutic protein biosimilar or interchangeable biosimilar combination products. For purposes of this guidance, the term presentation means **container closure systems**[2] (CCS) and device constituent parts.[3] Specifically, this guidance discusses data and information, including the design of studies, to support a demonstration of biosimilarity or interchangeability in an application or supplement submitted under section 351(k) of the Public Health Service Act (PHS Act) (42 U.S.C. 262(k)).[4] Additionally, this draft guidance expands on and clarifies the Agency's recommendations and expectations regarding the development of device constituent parts or container closure systems described in Q.I.4 of the guidance for industry entitled "Questions and Answers on Biosimilar Development and the BPCI Act" and the guidance for

[1] This guidance has been prepared by the Center for Drug Evaluation and Research (CDER) and the Center for Biologics Evaluation and Research (CBER) in cooperation with the Office of Combination Products in the Office of the Commissioner, and the Center for Devices and Radiological Health at the Food and Drug Administration.

[2] See the Glossary for definitions and usage of specific terms used throughout this guidance. Words found in the Glossary are bolded at first use.

[3] For brevity, we will use the term "presentation" throughout this guidance to refer to CCSs and device constituent parts. The scientific principles provided in this guidance also may apply to combination products with separately distributed constituent parts. A constituent part is the drug, device, or biological product part of a combination product (see 21 CFR 4.2).

[4] As part of the negotiations relating to the reauthorization of the Biosimilar User Fee Act (BsUFA), as described in "Biosimilar Biological Product Reauthorization Performance Goals and Procedures for Fiscal Years 2023 Through 2027" (BsUFA III goals letter), FDA agreed to issue guidance on "considerations for developing presentations, container closure systems, and device constituent parts for proposed interchangeable biosimilar biological products." The BsUFA III goals letter is available on the FDA website at https://www.fda.gov/media/152279/download.

industry entitled "Considerations in Demonstrating Interchangeability With a Reference Product" for biosimilar and interchangeable biosimilar products, respectively.[5]

In general, FDA's guidance documents do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

II. BACKGROUND

Section 351(k) of the PHS Act provides an abbreviated licensure pathway for biological products shown to be biosimilar to, or interchangeable with, an FDA-licensed reference product.[6] Section 351(k) of the PHS Act, as amended by the Biologics Price Competition and Innovation Act of 2009, sets forth the requirements for an application for a proposed biosimilar product and an application or a supplement for a proposed interchangeable product.[7]

Section 351(i)(2) of the PHS Act defines *biosimilarity* to mean "that the biological product is highly similar to the reference product notwithstanding minor differences in clinically inactive components" and that "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."

To meet the standard for *interchangeability*, an applicant must provide sufficient information to demonstrate biosimilarity and also to demonstrate that the biological product can be expected to produce the same clinical result as the reference product in any given patient and, if the biological product is administered more than once to an individual, the risk in terms of safety or diminished efficacy of alternating or switching between the 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.[8] Interchangeable biosimilar products may be substituted for the reference product without the intervention of the prescribing health care provider.[9]

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[5] When this guidance is finalized, the Agency intends to update section VIII., Considerations for Developing Presentations for Proposed Interchangeable Products, of the guidance for industry *Considerations in Demonstrating Interchangeability With a Reference Product* and to remove Q.I.4 of the guidance for industry *Questions and Answers on Biosimilar Development and the BPCI Act*.

[6] *Reference product* means the single biological product licensed under section 351(a) of the PHS Act against which a biological product is evaluated in a 351(k) application (section 351(i)(4) of the PHS Act).

[7] In this guidance, the following terms are used to describe biological products licensed under section 351(k) of the PHS Act: (1) *biosimilar* or *biosimilar product* refers to a product that FDA has determined to be biosimilar to the reference product (see sections 351(i)(2) and 351(k)(2) of the PHS Act), and (2) *interchangeable biosimilar* or *interchangeable product* refers to a biosimilar product that FDA has determined to be interchangeable with the reference product (see sections 351(i)(3) and 351(k)(4) of the PHS Act).

[8] See section 351(k)(4) of the PHS Act.

III. SCOPE

This guidance provides an overview of scientific considerations for developing presentations for proposed biosimilar and interchangeable biosimilar products. This guidance focuses on therapeutic protein biological products and provides an overview of important scientific considerations in demonstrating biosimilarity and interchangeability of a proposed therapeutic protein biological product in a particular presentation with a reference product in a particular presentation.

IV. GENERAL CONSIDERATIONS FOR EVALUATION OF PRESENTATIONS FOR PROPOSED BIOSIMILAR AND INTERCHANGEABLE PRODUCTS

When developing a product for licensure under section 351(k) of the PHS Act, it is important that sponsors carefully consider the presentation of the proposed product relative to the presentation of the reference product. The proposed presentation cannot result in a condition of use that has not been previously approved for the reference product or a dosage form, strength, or route of administration that is not the same as the reference product.[10]

The data and information needed to support licensure of a biosimilar or interchangeable biosimilar product may be influenced by the proposed product's presentation. This guidance provides a framework for sponsors to determine the types of data and information related to a proposed presentation that might be necessary to support licensure as a biosimilar or interchangeable product. The considerations described in this guidance are intended to provide clarity and support flexibility where appropriate and adequately justified.

V. QUALITY CONSIDERATIONS: CONTAINER CLOSURE SYSTEM, AND DEVICE CONSTITUENT PARTS

Expectations regarding product quality considerations for container closure systems and device constituent parts are generally the same for proposed biological products submitted in a marketing application submitted under section 351(a) of the PHS Act as for proposed biosimilar and interchangeable biosimilar products submitted in a marketing application under section 351(k) of the PHS Act.

A general description of the entire presentation should be provided in the chemistry, manufacturing, and controls (CMC) section of the application. There should be complete CMC

[9] See section 351(i)(3) of the PHS Act.

[10] See section 351(k)(2)(A)(i) of the PHS Act.

information for the proposed container closure system and any device constituent parts.[11] The BLA should include data from appropriate studies (e.g., extractable/leachable studies, performance testing, and stability studies)[12] that demonstrate compatibility between the device constituent part and the final formulation of the biologic constituent part. In addition, comparative in vitro performance testing data may be used to support the device constituent part of the proposed combination product. Applicants should refer to relevant FDA guidance documents and other resources that provide information on what data and information should be included to support the device constituent part(s) of the combination product. [13]

VI. CONSIDERATIONS FOR THE EVALUATION OF THE USER INTERFACE[14] FOR A COMBINATION PRODUCT

The use of a biological product generally involves a sequence of steps (i.e., tasks) because biological products are generally injected or infused into the body. These tasks can vary considerably depending on the type of presentation, and its **user interface,** including its design features. In addition, these products are prepared and administered by a variety of **end users**, including health care providers, patients, caregivers, or a combination of these end users.

The following sections describe FDA's recommendations for the comparative analyses conducted to identify and analyze differences in the user interface of a proposed biosimilar or interchangeable biosimilar combination product when compared with the user interface of its reference product.[15] These comparative analyses should be used in the development of the proposed user interface to identify whether additional data may be needed. FDA recommends that sponsors submit their comparative analyses for the final finished combination product (to-

[11] For the purposes of this guidance, the terms device and device constituent part are used interchangeably. For general information about combination products, see the guidance for industry and FDA Staff Principles of Premarket Pathways for Combination Products (January 2022) and https:www.fda.gov/combination-products.

[12] Guidance for industry *Container Closure Systems for Packaging Human Drugs and Biologics* (May 1999) and draft guidance for industry *Essential Drug Delivery Outputs for Devices Intended to Deliver Drugs and Biological Products* (June 2024)

[13] For additional guidance related to product development, see the FDA guidance web page to search for an FDA guidance document or to browse FDA guidance documents by topic. Information on these considerations may be found in applicable guidances. For example, for more information regarding injector delivery devices, see the guidance for industry and FDA staff *Technical Considerations for Pen, Jet, and Related Injectors Intended for Use with Drugs and Biological Products* (June 2013).

[14] The scientific principles described in this section may apply in cases where the product is not a combination product (e.g. a vial), in that case user interface also includes the container closure.

[15] This guidance does not apply to generic combination products. Applicants submitting an abbreviated new drug application under section 505(j) of the Federal Food, Drug, and Cosmetic Act for a generic combination product should instead refer to the draft guidance for industry *Comparative Analyses and Related Comparative Use Human Factors Studies for a Drug-Device Combination Product Submitted in an ANDA* (January 2017). When final, this guidance will represent the FDA's current thinking on this topic.

be-marketed commercial product) to the IND to receive FDA's input before submitting a biologics license application (BLA) or supplemental BLA.

Early communication with FDA through the IND may be particularly helpful if the sponsor is developing multiple strengths of the proposed product and seeks input on whether one set of complete comparative analyses focused on one strength may be sufficient to address the same user interface differences that appear in other strengths proposed in the 351(k) BLA.

A. General Framework for Recommended Analyses

This guidance recommends a stepwise, systematic approach for sponsors to use in identifying and analyzing differences in the user interface between a proposed biosimilar or interchangeable biosimilar combination product and the user interface of its reference product:

(1) First, sponsors should use the comparative analyses to identify all differences between the user interface of the proposed biosimilar or interchangeable biosimilar combination product and the user interface of the reference product.

(2) If the sponsor identifies any differences, the sponsor should next carefully consider whether any difference may impact a design feature that a user would rely on to perform a **combination product critical task**. Combination product critical tasks are those user tasks that if performed incorrectly, or not performed at all, would or could cause harm to the patient or user, where harm is defined to include compromised medical care.[16] For each task that may be impacted by a difference in the user interface, the applicant should evaluate the risk associated with **use errors** that may occur for those tasks. A sponsor may, for example, find a **use-related risk analysis**[17] to be a helpful tool for identifying combination product critical tasks that may be impacted by design differences and the use errors that may occur.

(3) As a final step, sponsors should classify each identified difference as a *minor design difference* if the difference does not impact a design feature that a user would rely on to perform a combination product critical task or as an *other design difference* if the difference may impact a design feature that a user would rely on to perform a critical task (see section B.3 Classify Identified Differences, below).

The discussion below further describes these three steps and considerations on when other design differences are identified.

[16] For additional information on critical tasks, see Q-5 in the guidance for industry and FDA staff *Application of Human Factors Engineering Principles for Combination Products: Questions and Answers* (September 2023).

[17] See draft guidance for industry *Purpose and Content of Use-Related Risk Analyses for Drugs, Biological Products (July 2024).*

B. Recommended Comparative Analyses To Identify Design Differences and Determine Whether They May Impact a Combination Product Critical Task

FDA recommends that sponsors use three types of comparative analyses to determine whether there are differences between the user interface design of the proposed biosimilar or interchangeable biosimilar combination product and its reference product. As noted above, to ensure differences between the user interfaces are adequately assessed, FDA recommends that sponsors conduct these analyses throughout the development process of the user interface of the final finished combination product. The comparative analyses that are submitted to FDA should reflect the proposed final finished combination product user interface.[18]

1. Conduct Comparative Analyses To Identify Design Differences

The following three types of analyses are recommended to compare the user interface of the proposed biosimilar or interchangeable biosimilar combination product with the user interface of its reference product:

(1) *Physical comparison of the device constituent part*: FDA recommends that the sponsor of the proposed biosimilar or interchangeable biosimilar combination product acquire the reference product and examine the physical features of the device constituent part for the proposed combination product and compare them with the reference product (e.g., visual, auditory, and tactile examination).[19] Sponsors should evaluate differences in the internal mechanics between a proposed biosimilar or interchangeable biosimilar combination product and its reference product to the extent they may impact a critical task associated with the use of the product (e.g., differences in force necessary to push a button to inject a product).

(2) *Comparative task analysis*: FDA recommends that sponsors conduct a comparative task analysis between the proposed biosimilar or interchangeable biosimilar combination product and its reference product. To conduct a comparative task analysis, sponsors should systematically dissect the use process for both the proposed combination product and the reference product and analyze and compare the sequential and simultaneous physical and cognitive activities for end users interacting with both products.

(3) *Labeling comparison*: FDA recommends a side-by-side, line-by-line comparison of the proposed labeling, including on-device labeling, carton labeling, information in the full prescribing information related to use of the device, the instructions for use, and

[18] For IND submissions that request assessment of comparative analyses, FDA recognizes that certain limited elements of the proposed user interface might not be identical to the final, to-be-marketed version (e.g., proposed product proprietary name). In addition, if a sponsor plans to submit a human factors protocol to FDA for IND review and anticipates that some limited elements of the user interface may change, they should identify which elements of the user interface are not yet finalized and seek Agency feedback on whether it would be acceptable to proceed with a human factors study before finalizing those elements. FDA intends to consider the acceptability of such an approach in the context of each proposed combination product.

[19] As appropriate, the physical comparison submitted to the IND should include high-resolution color images of the device constituent part of the proposed combination product and the device constituent part of the reference product and dimensions of the overall devices and of the components of the devices.

descriptions of the device constituent parts of the proposed biosimilar or interchangeable biosimilar combination product and its reference product.

2. Determine Whether Any Identified Difference May Impact a Design Feature That a User Would Rely on To Perform a Critical Task

For each of the three types of comparative analyses, the following outcomes are possible:

(1) *No design differences*: When no differences are identified between the user interface of the proposed biosimilar or interchangeable biosimilar combination product and the user interface of its reference product, it is likely that additional information and/or data about the user interface will not be necessary to support approval of the proposed combination product.

(2) *Differences in design*: If differences are identified between the design of the user interface of a proposed biosimilar or interchangeable biosimilar combination product and the design of the user interface of its reference product, the sponsor should evaluate whether those design differences may impact a design feature on which a user would rely to perform a critical task. As part of this evaluation, the sponsor should carefully evaluate the risk for use-related errors associated with each difference identified in the design of the user interface between the proposed biosimilar or interchangeable biosimilar combination product and its reference product and consider whether the proposed labeling mitigates any potential risk. The sponsor should consider the following[20]:

- The errors that users might commit or the tasks they might fail to perform
- The potential clinical consequences of use errors, considering the impact of the identified difference(s) in the context of the overall risk profile for the product
- Any mitigation strategies employed to reduce identified risks or eliminate **hazards**
- The context of use of the product (e.g., indication, user populations, use environment)

3. Classify Identified Differences

After evaluating the risk for use-related errors associated with each difference in design, the sponsor should categorize each difference as follows:

(1) *Minor design difference*: FDA views a design difference as minor if the difference between the user interface of the proposed biosimilar or interchangeable biosimilar

[20] In general, this type of information is typically considered in a use-related risk analysis. If sponsors elect to perform a use-related risk analysis during the development process, they may choose to provide that analysis to FDA along with the comparative analyses. See draft guidance for industry *Purpose and Content of Use-Related Risk Analyses for Drugs, Biological Products, and Combination Products* (July 2024).

combination product, in comparison to the user interface of its reference product, does not impact a design feature on which a user would rely to perform a critical task. A minor difference in design is likely to be viewed by FDA as acceptable, provided the information submitted in the sponsor's analyses demonstrates that the difference is in fact minor.

(2) *Other design difference*: FDA may not view a design difference as minor if any aspect of the comparative analyses suggests that the difference between the design of the user interface of the proposed biosimilar or interchangeable biosimilar combination product as compared with its reference product may impact a design feature on which a user would rely to perform a critical task.

C. Considerations When Other Design Differences Are Identified

Differences between the user interface of the proposed biosimilar or interchangeable biosimilar combination product and the user interface of its reference product may be acceptable provided that the design, labeling, and task differences are analyzed appropriately and that, when warranted, additional data and information beyond the comparative analyses are provided to demonstrate that the user interface differences do not preclude a showing that the proposed combination product meets the standards for biosimilarity or interchangeability, as applicable.

Early communication with FDA through the IND may be particularly helpful if the sponsor identifies a difference between the design of the user interface of the proposed biosimilar or interchangeable biosimilar combination product as compared with its reference product that may impact a design feature on which a user would rely to perform a critical task (i.e., an *other design difference*) and the sponsor would like FDA's feedback on whether additional information and/or data are warranted. For example, the sponsor should contact FDA if it determines that a critical task was modified, removed from, or added to the use process for the proposed biosimilar or interchangeable biosimilar combination product as compared with its reference product.

1. Biosimilar Products

After conducting comparative analyses such as those described in the sections above between the user interface of the proposed biosimilar combination product and the user interface of its reference product for the purposes of identifying what differences exist between the user interfaces and whether the same or similar risks may apply to the proposed combination product, if no differences or only minor differences exist, the sponsor may not need to submit additional data or information beyond the comparative analyses to the application.

If a design difference categorized as an *other design difference* is present in the final design of the user interface of the proposed combination product, the sponsor should consider whether information and/or data already exist that can demonstrate that potential use errors related to the design difference do not preclude approval of the proposed combination product as biosimilar to its reference product.

In some cases, if such information or data do not exist, an appropriately designed human factors validation study that includes existing or previous users of the reference product may be needed.

To inform the design of the human factors validation study, sponsors should conduct a comprehensive use-related risk analysis. The comprehensive use-related risk analysis should include a comprehensive and systematic evaluation of all the steps involved in using the proposed biosimilar combination product (e.g., based on a task analysis), the errors that users might commit or the tasks they might fail to perform, and the potential negative clinical consequences of **use errors** and task failures.[21]

Useful information can be obtained from the sponsor's own experience as well as from publicly available information sources such as adverse event reports and product safety communications.

2. Interchangeable Biosimilar Products

An interchangeable biosimilar product may be substituted for the reference product without the intervention of the health care provider who prescribed the reference product. Differences in the user interface between the proposed interchangeable biosimilar combination product and its reference product may raise uncertainty about whether the difference(s) would affect the ability of end users to use the interchangeable biosimilar product when it is substituted for the reference product without the intervention of the health care provider who prescribed the reference product.

Sponsors should conduct comparative analyses such as those described in the sections above between the user interface of the proposed interchangeable biosimilar combination product and the user interface of its reference product for the purpose of identifying what differences exist between the user interfaces and whether the same or similar risks may apply to the proposed combination product.

If no differences or minor differences exist, the sponsor may not need to submit additional data or information beyond the comparative analyses to support the application.

If a design difference categorized as an *other design difference* is present in the final design of the user interface of the proposed interchangeable biosimilar combination product, the sponsor should consider whether information and/or data already exist that can demonstrate that potential use errors related to the design difference do not preclude a showing that the proposed combination product meets the standards in sections 351(k)(4)(A) and (B) of the PHS Act.[22] For example, a sponsor may already have data that may help further characterize the impact of a design difference.[23] As an additional example, when evaluating the risk for use-related errors

[21] See draft guidances for industry *Purpose and Content of Use-Related Risk Analyses for Drugs, Biological Products, and the final Application of Human Factors Engineering Principles for Combination Products: Questions and Answers (2023).*

[22] The standards in sections 351(k)(4)(A) and (B) of the PHS Act are described in Section II of this guidance.

[23] For example, a sponsor may develop a proposed combination product's pen injector with an ergonomic design feature that orients the hand such that the resulting angle of injection is 90°, which differs from the 45° angle of

associated with the difference in design between the proposed interchangeable biosimilar combination product and its reference product, the sponsor may be able to point to the context of use of the product to demonstrate that the difference in design will not preclude a showing that the proposed interchangeable product meets the standards in sections 351(k)(4)(A) and (B) of the PHS Act.

In some cases, if existing information or data are not available, FDA may request that sponsors provide additional information and/or data (e.g., in vitro data, data from a comparative use human factors study or an appropriately designed human factors study, or other scientific information) to demonstrate that the difference in design does not impact a critical task or, if the difference in design may impact a critical task, that potential use errors related to the difference do not preclude a showing that the proposed interchangeable biosimilar combination product meets the standards in sections 351(k)(4)(A) and (B) of the PHS Act. Based on the additional information or data, FDA will determine whether the applicant has demonstrated that the design difference between the user interface of the proposed combination product and its reference product is acceptable for a proposed interchangeable biosimilar combination product.

VII. CONSIDERATIONS FOR APPLICANTS PROPOSING A PRESENTATION FOR WHICH ITS REFERENCE PRODUCT IS NOT MARKETED

If an applicant intends to develop and seek licensure of a proposed combination product in a different presentation than its reference product, it is likely that there will be differences between the user interface of the applicant's proposed combination product and its reference product.

A. Biosimilar Products

Some design differences in the presentation of the proposed biosimilar combination product compared with its reference product may be acceptable, as long as the proposed combination product meets the standards for biosimilarity, including that such differences would not result in a condition of use that has not been previously approved for its reference product or a dosage form, strength, or route of administration that is not the same as that of its reference product. It may be possible, for example, for an applicant to obtain licensure of a proposed biosimilar combination product with a prefilled syringe or an auto-injector presentation, even if the presentation of its reference product is a vial, provided that the proposed biosimilar combination

injection for its reference product. Based on the comparative analyses, a sponsor should conclude that there is a difference that may impact a design feature on which a user would rely to perform a critical task and should characterize it as an *other design difference*. However, the sponsor's existing in vitro testing, when compared with its reference product, may demonstrate that even if a user injects at a 45° angle instead of the intended 90° angle, there is no difference in the dose delivery of the proposed combination product as compared to its reference product notwithstanding the difference in ergonomic design. FDA will consider on a case-by-case basis whether this type of data may be sufficient to conclude that the design difference does not preclude a finding of interchangeability between the proposed combination product and its reference product.

product meets the statutory standards for biosimilarity.[24] Additionally, human factors study data may be needed.

However, an applicant will not be able to obtain licensure of a proposed biosimilar product when a design difference in the presentation results in any of the following:

- A clinically meaningful difference between the proposed biosimilar product and its reference product in terms of safety, purity, and potency
- A different route of administration, dosage form, or strength
- A condition of use (e.g., indication, dosing regimen) for which its reference product has not been previously approved
- A proposed biosimilar product that otherwise does not meet the standards for biosimilarity

B. Interchangeable Products

As part of the information required to support licensure of the combination product as an interchangeable biosimilar product, FDA expects that additional information and/or data (e.g., data from in vitro studies, data from a comparative use human factors study or an appropriately designed human factors study) will be needed to characterize any impact of the differences and to evaluate whether any of the differences between the proposed combination product and its reference product preclude licensure of the proposed combination product as an interchangeable biosimilar product. Sponsors are encouraged to contact FDA early during product development to discuss the proposed presentation and specific considerations regarding the additional information and/or data proposed.[25]

VIII. LIFE CYCLE CONSIDERATIONS

The life cycle considerations discussed in this section refer only to the presentation.[26] For a product that has been licensed as a biosimilar product, when seeking licensure of the product as an interchangeable biosimilar, the outcome of the comparative analyses described in section VI will determine whether additional information may be needed to support a demonstration that the proposed product can be expected to produce the same clinical result as its reference product in

[24] Additionally, as a scientific matter, adequate performance data for the presentation should be provided and the presentation must be shown to be compatible for use with the final formulation of the proposed biosimilar biological product through appropriate studies, including, for example, extractable/leachable studies and stability studies. See 21 CFR 211.84, 211.94, and part 4.

[25] See guidance for industry *Formal Meetings Between the FDA and Sponsors or Applicants of BsUFA Products (July 2025)*.

[26] When establishing the quality target product profile, sponsors should consider the product's life cycle management.

any given patient and that the risk in terms of safety or diminished efficacy of alternating or switching between use of the proposed product and its reference product is not greater than the risk of using the reference product without such alternation or switch.[27]

[27] For sponsors who are considering licensure of their product as an interchangeable biosimilar product, it may be feasible to develop a single human factors study that is appropriately designed to support licensure of the proposed combination product as both biosimilar and interchangeable. We encourage early interaction with the Agency to discuss the design of the proposed human factors study.

GLOSSARY

Container closure system: The sum of packaging components that together contain and protect the dosage form. This includes primary packaging components and secondary packaging components if the latter are intended to provide additional protection to the drug product. A packaging system is equivalent to a container closure system.[28]

Combination product critical tasks: Those user tasks that if performed incorrectly, or not performed at all, would or could cause harm to the patient or user, where harm is defined to include compromised medical care.[29]

Hazard: Potential source of harm.[30]

Use error: User action or lack of action that was different from that expected by the manufacturer and caused a result that (1) was different from the result expected by the user and (2) was not caused solely by device failure and (3) did or could result in harm.[30]

Use-related risk analysis: The systematic use of available information to identify use-related hazards and to estimate the use-related risk.[29]

User/end user: Person who interacts with (i.e., operates or handles) the device.[30]

User interface: The user interface for a combination product includes all points of interaction between the combination product and the user(s), including displays, controls, packaging, product labels, carton labeling, instructions for use, and training, if applicable.[29]

[28] See guidance for industry *Container Closure Systems for Packaging Human Drugs and Biologics.*

[29] See guidance for industry *Application of Human Factors Engineering Principles for Combination Products: Questions and Answers.*

[30] See guidance for industry *Applying Human Factors and Usability Engineering to Medical Devices* (February 2016).