

- The biological product has the same route of administration, dosage form, and strength as the reference product.
- The biological product is manufactured, processed, packed, or held in a facility that meets standards designed to assure that the biological product continues to be safe, pure, and potent.

4.2.5 351(k) information on biosimilarity

The PHSA requires that a 351(k) application include, among other things, information demonstrating biosimilarity based on data derived from the following:

- Analytical studies demonstrating that the biological product is highly similar to the reference product notwithstanding minor differences in clinically inactive components
- Animal studies (including the assessment of toxicity)
- A clinical study or studies (including the assessment of immunogenicity and PK or PD) that are sufficient to demonstrate safety, purity, and potency in one or more appropriate conditions of use for which the reference product is licensed and for which licensure is sought for the biosimilar product

Note: The FDA may determine, in its discretion, that an element described above is unnecessary in a 351(k) application.

4.2.6 Licensure

The FDA shall license the biological product under Section 351(k) of the PHSA if the FDA determines that the information submitted in the application (or supplement) is sufficient to show that

- The biological product is biosimilar to the reference product; or
- The biological product meets the standards described in 351(k)(4) and is, therefore, interchangeable with the reference product; and
- The applicant (or another appropriate person) consents to the inspection of the facility, in accordance with Section 351(c).

Note: The BPCI Act does not require that the FDA promulgate guidance or regulation before reviewing or approving a 351(k) application.

4.2.7 Reference product

The PHSA defines the *reference product* for a 351(k) application as the “single biological product licensed under section 351(a) against which a biological product is evaluated.”

- Data from animal studies and certain clinical studies comparing a proposed biosimilar product with a non-U.S.-licensed product may be used to support a demonstration of biosimilarity to a U.S.-licensed reference product.