Appendix H: Biosimilars

KEY TERMS

1. What is a reference product?
   a. The single biological product, already approved by the Food & Drug Administration (FDA), against which a biosimilar product is compared
   b. Also referred to as an “originator product”

2. What is a biosimilar?
   a. A biological product that is highly similar to the FDA-approved reference product notwithstanding minor differences in clinically inactive components
   b. There are no clinically meaningful differences between biological product and the reference product in terms of safety, purity and potency

3. What does “highly similar” mean?
   a. High similarity is demonstrated by analyzing the structure and function of both the reference product and the biosimilar
   b. Slight differences are expected during the manufacturing process for biological products

4. What does “clinically meaningful differences” mean?
   a. Generally proven through human pharmacokinetic and pharmacodynamic studies, an assessment of clinical immunogenicity, and if required by the FDA, additional clinical studies
   b. Examples of clinically meaningful differences include: differences in expected range of safety, purity, or potency

5. What does “interchangeability” mean in terms of biosimilars?
   a. Interchangeability status is a second level of FDA approval beyond biosimilarity and is only granted if: (1) additional clinical trials demonstrate that the biosimilar can produce the same clinical result as the reference product in any given patient, and (2) additional clinical trials demonstrate the risk to efficacy or safety with alternating or switching between the biosimilar and reference product is not greater versus consistent use of the reference product
   b. There are currently no interchangeable FDA approved biosimilar products at this time

6. Can a biosimilar be substituted for a reference product?
a. Biosimilar drugs may be substituted for the reference product, based on state laws. Additional considerations include individual institutional practice and physician approval for substitution.

NOMENCLATURE & LABELING
1. The naming of biosimilars requires the assignment of a four-character alphabetic suffix to the nonproprietary name of the original product to distinguish between reference medications and their biosimilar.
   a. Example:

   ![Diagram of biosimilar naming]

   - **Proprietary Name**: Kanji® (Trastuzumab-ans)
   - **Core Name**: Component shared among reference product and biosimilar product as part of the proper name of those products
   - **Suffix**: Unique, four letters and devoid of meaning used to help identify the manufacturer of a biosimilar

NATIONAL COMPREHENSIVE CANCER NETWORK® (NCCN®) APPROACH
1. The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) are developed by panel members from NCCN member institutions. Recommendations for allowance of biosimilar substitution for reference products may or may not be included in each guideline based on panel member recommendations, clinical experience, and current evidence-based data.
   a. NCCN Guidelines® include the following footnote on the reference product:
      i. An FDA-approved biosimilar is an appropriate substitute for … (reference product)
   b. NCCN Chemotherapy Order Templates (NCCN Templates®) include the following note under the reference product in the Chemotherapy Regimen section:
      i. A biosimilar agent may be substituted if clinically appropriate. For more information on the use of biosimilars, please refer to disease-specific guideline.
   c. NCCN Drugs & Biologics Compendium (NCCN Compendium®) includes separate entries for each FDA-approved biosimilar according to disease-specific guidelines.

REFERENCES
