In general, we expect injectable biological products to have both the same total content of drug substance (in mass or units of activity in a container closure) and the same concentration of drug substance (in mass or units of activity per unit volume) as the reference product to have the same "strength" under section 351(k)(2)(A)(i)(IV) of the PHS Act. We note, however, that for certain complex biological products, a modified approach may be needed.

The total content of drug substance generally should be expressed using the same measure as the reference product. For example, if the strength of the reference product is expressed as milligrams (mg) per total volume in a container closure, for example, mg/five milliliters (mL), the proposed biosimilar product generally should also describe its strength in mg/five mL, rather than units per five mL. If the total content of drug substance is expressed in units of activity (e.g., international units [IU] or units per total volume in a container closure), the units of the proposed biosimilar product should be the same as the reference product.

The concentration of the drug substance (in mass or units of activity per unit volume) generally should be expressed using the same measure as the reference product. The extinction coefficient used to calculate the concentration of a protein drug substance should be determined experimentally, and justification for the experimental method should be provided. If the proposed biosimilar product is a dry solid (e.g., lyophilized) from which a constituted or reconstituted solution is prepared, then the 351(k) application should contain information demonstrating that the concentration of the proposed biosimilar product, when constituted or reconstituted, is the same as that of the reference product.

The requirement for a 351(k) application to contain information demonstrating that the proposed product and the reference product have the same "strength" applies to both biosimilar products and interchangeable products.

Q. I.13: What constitutes "publicly-available information" regarding FDA's previous determination that the reference product is safe, pure, and potent to include in a 351(k) application?

A. I.13 (Proposed Answer): "Publicly-available information" in this context generally includes the types of information found in the "action package" for a BLA (see section 505(l)(2)(C) of the FD&C Act). However, the FDA notes that submission of publicly available information composed of less than the action package for the reference product BLA will generally not be considered a bar to submission or approval of an acceptable 351(k) application.

The FDA intends to post on the Agency's Web site publicly available information regarding FDA's previous determination