

3.13.3 Potential benefits of new measurement standards

With the development of new analytical methods comes the need for new standards to evaluate them. The term *standard* can apply to measurements or to processes, and although process standards are valuable in ensuring effective manufacturing process operation and validation, the measurement standards need to be revisited. A measurement standard can be standardized test materials used to evaluate the performance of a measurement method, or it can be a particular analytical procedure used to take a measurement. Standardized test materials can be used to assess the precision and the accuracy of many different analytical technologies and are, thus, more likely to foster competition and development of new and improved analytical methods by industry and academia. Standard test materials could be used to verify the ability of an analytical method to detect differences between product batches from a single manufacturer or products from different manufacturers. For example, if a method is being developed to assess the sugars attached to a protein, the analytical method could be used to test a set of related standard test materials in order to determine the precision and the accuracy of the method. In this way, a given technology can be optimized, or a variety of different technologies can be compared for their ability to accurately and quantitatively assess the quality of a product. The development of such measurement standards would also be extremely valuable for ensuring that current and future analytical methods are properly working and are providing consistent results from assay to assay and from lab to lab.

3.13.4 Three specific properties needing improved measurement

The FDA has identified three properties of therapeutic proteins that cannot be sufficiently measured at this time, but are very important for understanding the behavior of protein drugs. Improved analytical methods to measure these three properties would be particularly useful in determining the extent of similarity of biological protein products intended to be similar.

3.13.4.1 Posttranslation modifications As previously indicated, proteins contain added structural features, such as attached sugar chains, that may be critical for their clinical activity. These attached modifications can be complex and heterogeneous, and we currently lack standardized analytical methods to qualitatively and quantitatively assess the structure as it relates to the intact protein and understand the relationship of the modifications to potency and clinical performance. We are particularly interested in better methods for analyzing the sugars (glycosylation) and other modifications known to affect the medicinal activity of these products.