International Alliance for Biological Standardization

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Clinically Relevant Specifications – A Regulatory Perspective

Traditionally, specifications are set as a final check that the biologic drug product is representative of the marketing authorization and are intended to ensure that a product is safe and efficacious when used as labeled. Often, setting specifications is primarily based on manufacturing experience from a limited number of batches at the time of the marketing application. This approach may not wholly represent the true safety and efficacy of the drug and creates a challenge for both industry and regulators in defining and authorizing appropriate specifications that support the product lifecycle and supply to patients. Establishing acceptance criteria based on manufacturing experience may result in limits that are narrow and lead to unnecessary batch rejection. In contrast, establishing acceptance criteria based on statistical analysis of a limited number of batches may result in limits that are broad and lead to inappropriate lot release. Comprehensive approaches are needed to define the most appropriate specifications. One such approach has been coined clinically-relevant (or patient-centric). Clinically relevant specifications have been defined as a set of criteria and acceptance ranges to which drug products should conform to deliver the therapeutic benefit indicated in the label. The resultant specifications often extend beyond the manufacturing experience. From a regulatory perspective, the setting of specifications should consider all available data to ensure that decisions regarding the suitability of the product appropriately includes the line between rejecting lots that are likely to perform as expected and releasing lots that fail to meet the expectations. The justification should be supported by additional sources of data such as structure-function data, in vitro data, platform experience, or prior knowledge. The presentation will focus on the regulatory experience and expectations when setting biologic product specifications that exceed the manufacturing experience at the time of the market application.