Specifications - too wide or too narrow? The age-old debate between regulators and industry, and how we can move forward.

Sean Barry, Health Products Regulatory Authority, Ireland

For products in early access programmes, accelerated approval pathways, or for orphan products used to treat rare diseases, there are often a limited number of batches available at the time of licencing. This creates a challenge for both industry and regulators in defining appropriate specification acceptance criteria. In such scenarios, establishing acceptance criteria based on manufacturing capability or clinical qualification would likely result in limits which are too narrow and lead to unnecessary batch rejection during the lifecycle of the product. In contrast, acceptance criteria derived solely from statistical analysis of a limited number of batches could result in specification limits which are too broad and cannot be justified clinically. Therefore new approaches are needed to define the most appropriate specifications. For example, justifications could be based on additional sources of information such as in vitro data, or prior knowledge either specific to a development platform or from related development programs. Ultimately it must be justified that the final registered limits will result in a safe and efficacious product. However there is no single agreed approach on how such justifications should be presented in regulatory filings, and a global approach is needed to harmonise regulatory expectations.