Setting Internal Release Limits from accelerated stability data in vaccine early formulation development phase.

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Abstract

Internal Release Limits (IRLs) are a release windows to be applied at the time of manufacture to ensure that all material released within this range will remain within specification limits until the end of the expiry period. Such release windows are narrower than specification limits to consider the degradation of the product, uncertainty about the slope estimate, and measurement error. Interestingly, specification limits and shelf-life must be approved by authorities with relatively rigid data requirements and methods, while IRLs are at the manufacturer discretion, which allow the use of innovative methodologies.

IRLs usually require several batches monitored in stability over several years to get a realistic estimation of the product behavior and may only be computed in mature products. Unfortunately, this makes this methodology difficult to implement in new products with not enough data are available to compute realistic IRLs. As a result, some teams understand only late in their drug development that the release window will be too tight to ensure a viable manufacturing in case of unforeseen stability issues.

Recently new methods allowing to predict vaccine stability more efficiently and more quickly than current methods using data from accelerated stability studies have been published. Using innovative approaches such as Bayesian statistics and Advanced Kinetic Modelling (AKM), one of the aim of the Inno4Vac project (www.inno4vac.eu/) is to quickly estimate in what range a product should be released to stay within the specifications over its expiry period based on short term accelerated stability data. This strategy will contribute to early detect in vaccine development potential issue with the setting of specification limits and to avoid difficult negotiations with authorities a couple of years after submission, when stability problems typically appear.