PALL Biotech

Technical Regulatory Topic

Definition of Batch and Lot in Continuous Bioprocessing

Continuous Processing

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Introduction

One of the most common questions related to continuous bioprocessing is the definition of a lot or a batch. This is driven by the fact that the vast majority of the current biomanufacturing processes rely on batch processing steps and hence the definition of a lot or a batch is naturally related to the manufacturing schedule.

Regulatory Background

From regulatory perspective, the end-user has significant freedom to define the batch or lot:

21 CFR Part 210.3 Definitions:

(2) Batch means a specific quantity of a drug or other material that is intended to have uniform character and quality, within specified limits, and is produced according to a single manufacturing order during the same cycle of manufacture.

(10) Lot means a batch, or a specific identified portion of a batch, having uniform character and quality within specified limits; or, in the case of a drug product produced by continuous process, it is a specific identified amount produced in a unit of time or quantity in a manner that assures its having uniform character and quality within specified limits.[1]

Considerations

The regulatory expectations with respect to a batch or a lot are applicable to continuous bioprocessing. This means that a batch or a lot can be a certain (predefined) quantity of product produced, or a quantity of product produced during a (predefined) time interval. This could also be related to the use of auxiliary materials, such as filters, single-use assemblies, etc.

In this respect, one could consider a strategy where the definition of a lot is based on a risk assessment and the batch or lot definition is tied to the most relevant risk. If that risk is associated with the use of some auxiliary materials (e.g. a bag or a filter) that is to be swapped out periodically, one might consider relating the definition of a lot or batch to the use of such auxiliary material.

Continuous downstream processing systems occasionally have a cyclic nature. This is – for instance – true for all continuous chromatography systems, in which multiple columns undergo the same sequence of events in a cyclic way. In case the most relevant risk is associated to such a cyclic process, one could also consider using (a multiple of) the cycle time as a starting point for the definition of sub-lots, lots or batches. This provides the additional advantage that consistency between subsequent sub-lots is inherently built into the definition.

Hybrid Manufacturing Platforms

Although the integrated end-to-end continuous platform may be the ultimate manifestation of a continuous biomanufacturing, quite a few companies have presented examples of hybrid processes. Such hybrid processes rely on a combination of batch process steps and continuous process steps. The most common hybrid process relies on (repetitive) fed batch cell culture and clarification, combined with continuous capture and subsequent polishing steps. Occasionally, final ultrafiltration and diafiltration steps are performed in a (repetitive) batch mode.

In these cases, the more traditional approaches towards batch definitions, for example tied to the amount of product produced in one bioreactor, could still be applied.

Literature References

[1] Code of Federal Regulations: 21 CFR 210.3 (Definitions), Title 21, Volume 4 (revised April 1, 2019).

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