

PRESENTATION ABSTRACT

Presentation topic: Lyophilization process control past and future

Speaker:

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Presentation abstract:

A lyophilization process is usually only specified in terms of a 'recipe' (shelf temperature and chamber pressure vs. time). This, however, may not guarantee repeatable conditions for the freezing and sublimation steps. According to a QbD (Quality-by-Design) approach, there is the need to study in depth the process in order to develop on-line tools to enable better monitoring and control. It is necessary to move from intensive property (independent of mass) measurements (such as temperature, pressure –partial or total-) to parameters which are scalable and in so doing implement the necessary tools to control the parameters and hence the cycle; thus permitting real-time feedback control actions. Two variables are key to monitoring the lyophilization process: sublimation interface temperature (during the whole of primary drying this has to be maintained below the collapse temperature) and sublimation mass flow (which has to be maximized to achieve the most cost effective cycle). With classical monitoring tools these key goals are not achievable.

The presentation is comprised of three main elements:

- The first element presents an overview of the classical process validation with its limitations and the main improvements driven, first, by the 2004 FDA PAT Guideline and, second, by the newer QbD approach.
- The second element presents a technique for monitoring a group of process variables without the need to physically insert a probe. In many engineering applications it is desirable to have estimates of hard-to-measure or even non-measurable quantities. An observer combines a prior knowledge of the physical system (mathematical model) with experimental data (in-line measurements) to provide an in-line estimation of the desired quantities.
- The final element demonstrates how the monitored variables can be used to close the loop, enabling an in-line feedback control with a predictive action.

A case study involving a lyophilization process will be presented. Results just monitoring a production cycle and also a full automatic closed-loop control cycle will be shown where the only input is the maximum allowable product temperature, from which the software calculates the shelf temperature required to achieve this; reaching it as fast as possible without overshoots.