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Parametric Release of Pharmaceutical and Medical Device Products Terminally Sterilized by Moist Heat

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PDA Task Force on Technical Report No. 30: Parametric Release of Pharmaceutical and Medical Device Products Terminally Sterilized by Moist Heat

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1.0 Introduction

Parametric release is a sterility assurance release program that is founded upon effective control, monitoring, and documentation of a validated sterile product manufacturing process where sterility release is dependent upon demonstrated achievement of critical operational parameters in lieu of end product sterility testing. In this program, critical operational parameters and performance attributes are determined for process steps that occur prior to and during the performance of the sterilization process. The parametric release program is based on effective process control, monitoring, and documentation as well as a thorough understanding of the validated moist heat sterile product manufacturing process. A validated moist heat sterilization process must deliver a probability of a non-sterile unit (PNSU)[i] that is less than or equal to 10^{-6} for pharmaceutical and medical device products.[ii]

The previous version of *PDA Technical Report No. 30: Parametric Release of Pharmaceuticals Terminally Sterilized by Moist Heat* was published in 1999. Since 1999, many regulatory agencies and pharmacopoeial organizations across the globe have recognized the use parametric release and have fostered its implementation through the development of supporting standards, guidances and recommended practices. This growing adoption of parametric release necessitated an update to the 1999 report. This update provides current demonstrated best practices of this sterile product release method with an emphasis on use of science-based approaches during the development of a parametric release program for pharmaceutical and medical device products terminally sterilized by moist heat.

The sterility test has been widely used as the primary sterile product release criterion for moist heat sterilized pharmaceutical products and medical devices for many years. However, the sterility test is limited in its sensitivity and lacks statistical significance for the evaluation of sterility for terminally sterilized products given the exceedingly low probability of detection of contaminated units ***(1).*** The lack of statistical significance of the sterility test is summarized in **Appendix A** through a probability analysis of detecting sterility test positives with various contamination rates and sample sizes.

As a result of the limitations of the sterility test, the parametric release program has been developed as a proactive and science-based alternative to post-process (reactive) sterility testing for sterile product release. With parametric release, an acceptable sterility test cannot be used to support release for sterile products where one or more critical operational parameters have not been met.

The moist heat sterilization process is well-suited for the parametric release program because:

- it is well understood and dependable
- it is easily controlled and validated
- it is universally recognized for its effectiveness
- it delivers broad spectrum lethality (molds, yeasts, bacteria/spores, viruses)
- lethality can be mathematically modeled

The task force that participated in the development of this technical report was comprised of industry scientists, microbiologists and engineers from regions across the globe to ensure scientifically sound best practices were presented regarding parametric release of moist heat sterilized pharmaceutical products and medical devices.

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[i] Since Sterility Assurance Level (SAL) defines sterility in terms of probability of non-sterility, PNSU will be used in this report since *this term* accurately reflects this expression.

[ii] Although not acceptable for use with drugs, it is recognized that a PNSU of $\leq 10^{-3}$ is adequate in some regions for certain low risk medical devices (e.g., where intended use includes non-compromised tissue contact with devices such as gowns and towels).