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New Sterilization Requirements: new Annex 1 EU GMP (steam requirements)

INTRODUCTION

In order to update the current regulatory and technological environment in the manufacture of sterile medicinal products, EU GMP Annex 1 has been revised. After almost 5 years of waiting since the first draft in 2017 and another 2 years since the second draft in 2020 with the review of the respective public comments, the EU Commission published on August 22 the long-awaited Annex 1 of the EU GMP on "Manufacture of sterile medicinal products".

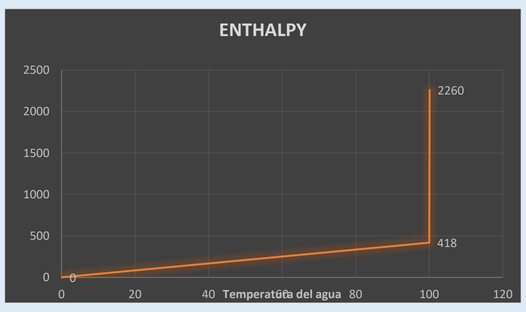
The new annex clarifies how manufacturing companies can take advantage of new possibilities resulting from the implementation of a better understanding of the risk management process (ICH Q9 - Quality Risk Management) and the pharmaceutical quality system (ICH Q10 - Pharmaceutical Quality System). It also includes new technological developments that required revision of Annex1.

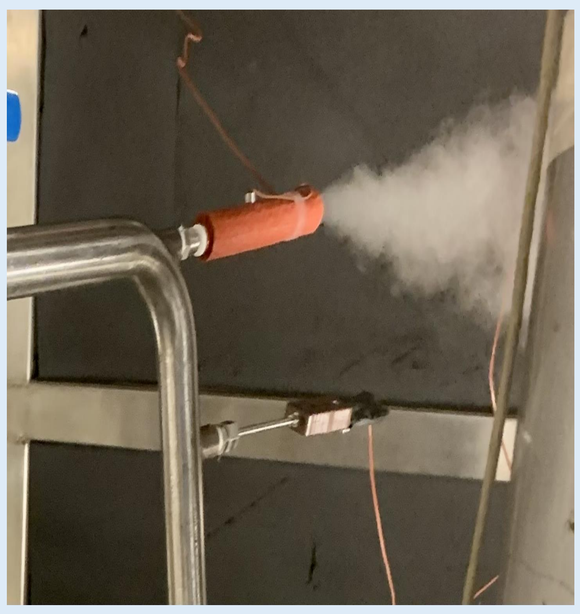
The revision of Annex 1 also takes into account changes in other GMP chapters and annexes and/or links them together for further control (Chapter 1 - Pharmaceutical Quality System, Annex 4 on Manufacture of veterinary medicinal products other than immunological veterinary medicinal products, Annex 12 on Use of Ionizing Radiation in the manufacture of medicinal products, Annex 15 on Qualification and Validation, Annex 17 on Parametric Release), as well as other related regulations (ISO 14644).

CRITICAL PROCESS PARAMETERS IN STERILIZATION (STEAM REQUIREMENTS)

SUPERHEATING

When the steam is superheated, the heat (energy) released by the steam when it cools (does not condense) in contact with the body to be sterilized is less than the latent heat of condensation (typical formation of condensate in autoclaves).





DRY FRACTION

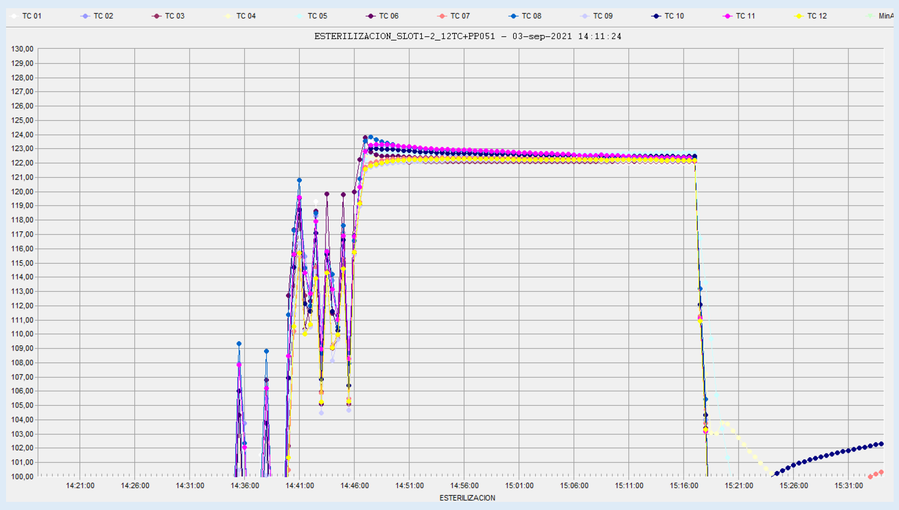
When the dry fraction is low, the condensed water acts as an insulator and hinders the transfer of heat (energy) to the body or substance that receives it. In addition, it evaporates on contact with steam, producing the opposite effect.

NON-CONDENSABLE GASES

Non-condensable gases act as insulators since the steam does not come into contact with the product.
Due to this, the adequate sterilization conditions (lower temperatures at high pressures) are not reached.

THERMAL MAPPING

The thermal mapping of the loads and the surfaces that must be sterilized in any installation is very important because the penetration of the steam and the measurement of its sterilizing efficacy are the most critical aspects in achieving the sterilization assurance level (SAL, 10exp-6).



CONCLUSION

Compared to the previous 2020 draft, the basic structure of Annex 1 remained unchanged, but the new revision is more comprehensive, increasing from 52 to 58 pages, and there are numerous deletions, summaries, and new insertions in many chapters.

For example, the subchapter "Barrier Technologies" in Chapter 4 "Facilities" is almost doubled to address in greater detail the use of gloves and materials as well as decontamination methods in RABS and isolators separately, and the subchapters "Form-Fill-SEAL (FFS)" and "Blow-Fill-Seal" (equipment used in the manufacture of sterile finished products) in Chapter 8 "Production and Specific Technologies" almost triple in content. In this presentation we would like to present and discuss some relevant aspects, emphasizing the sterilizing steam new requirements related to the processes of sterile finished products. We will also review some of the most important qualification methods.

Does your company comply with the new requirements of Annex 1 regarding sterilization?
Do you know all the risks associated with your sterile manufacturing process?
Do you know what tests you should carry out to implement the management of these risks and minimize their prevalence?
What is the sterilization method you use in your production equipment? Have you validated this method according to the requirements of the new annex 1?

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REFERENCES

- Annex 1_GMP (ver.2022)
- cGMPs
- European Pharmacopeia