GMP Annex 1 Changes

Annex 1 has been released by the EU.

After being issued in 1992, and not updated since 2008, its revision was prompted by several factors. These include:

- The consideration of new technologies and processes
- The inclusion of advanced principles such as quality risk management (QRM)
- Aligning standards with WHO, FDA etc.
- Statements of non-compliance with GMP in relation to sterile manufacturing
- Recalls that have happened due to contamination or sterility failures.

Previously Annex 1 only addressed cleanroom qualification and classification however now cleanroom monitoring and risk management will be emphasized, with your ‘Contamination and Control Strategy’ (CCS) much more developed. The CCS should be comprehensively documented and supported in validated manufacturing and control methods. The development of the CCS requires thorough technical and process knowledge and elements to be considered within the documentation include (but are not limited to):

- Premises, equipment, personnel, and utilities
- Raw material controls
- Product containers and closures
- Process risk assessment and validation
- Equipment, utilities, and premises maintenance
- Cleaning and disinfection
- Monitoring and prevention systems.

The CCS should be periodically reviewed and updated as needed in order to drive improvement.

Another area that gains importance is the Pharmaceutical Quality System (PQS). The manufacturer's PQS should encompass and address the specific requirements of sterile product manufacture and ensure that all activities are effectively controlled so that microbial, particulate and pyrogen contamination is minimized in sterile products.

Aseptic process simulation (APS), also known as 'Media Fill' is one of the other main topics in the revision. APS is applicable to filtered liquids as well as non-filterable formulations, sterile powders, lyophilised products and production campaigns. Updated guidance is provided on the critical manufacturing steps and expected interventions that should be included during the APS exercises, including factors that should be considered when developing the APS plan and the initial validation and re-validation.

Several new requirements and clarity of existing aspects are all included in the revision of Annex 1 and implementing the guidance will be key. A copy of the draft revision can be found here and it is expected to be implemented later in 2022 or early next year.