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Title: Parametric Release

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Note that this document has been prepared in association with PIC/S. It should be read in conjunction with CPMP/QWP/3015/99 Note for Guidance on Parametric Release which was adopted by the CPMP in February 2001. See http://**www.emea.eu.int/htms/human/qwp/qwpfin.htm**

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1. Principle

1.1 The definition of Parametric Release used in this Annex is based on that proposed by the European Organization for Quality: " A system of release that gives the assurance that the product is of the intended quality based on information collected during the manufacturing process and on the compliance with specific GMP requirements related to Parametric Release."

1.2. Parametric release should comply with the basic requirements of GMP, with applicable annexes and the following guidelines.

2. Parametric release

2.1. It is recognised that a comprehensive set of in-process tests and controls may provide greater assurance of the finished product meeting specification than finished product testing.

2.2. Parametric release may be authorised for certain specific parameters as an alternative to routine testing of finished products. Authorisation for parametric release should be given, refused or withdrawn jointly by those responsible for assessing products together with the GMP inspectors.

3. Parametric release for sterile products

3.1. This section is only concerned with that part of Parametric Release which deals with the routine release of finished products without carrying out a sterility test. Elimination of the sterility test is only valid on the basis of successful demonstration that predetermined, validated sterilising conditions have been achieved.

3.2. A sterility test only provides an opportunity to detect a major failure of the sterility assurance system due to statistical limitations of the method.

3.3. Parametric Release can be authorised if the data demonstrating correct processing of the batch provides sufficient assurance, on its own, that the process designed and validated to ensure the sterility of the product has been delivered.

3.4. At present Parametric release can only be approved for products terminally sterilized in their final container.

3.5. Sterilization methods according to European Pharmacopeia requirements using steam, dry heat and ionising radiation may be considered for parametric release.

3.6. It is unlikely that a completely new product would be considered as suitable for Parametric Release because a period of satisfactory sterility test results will form part of the acceptance criteria. There may be cases when a new product is only a minor variation, from the sterility assurance point of view, and existing sterility test data from other products could be considered as relevant.

3.7. A risk analysis of the sterility assurance system focused on an evaluation of releasing non-sterilised products should be performed.

3.8. The manufacturer should have a history of good compliance with GMP.

3.9. The history of non sterility of products and of results of sterility tests carried out on the product in question together with products processed through the same or a similar sterility assurance system should be taken into consideration when evaluating GMP compliance.

3.10. A qualified experienced sterility assurance engineer and a qualified microbiologist should normally be present on the site of production and sterilization.

3.11. The design and original validation of the product should ensure that integrity can be maintained under all relevant conditions.

3.12. The change control system should require review of change by sterility assurance personnel.

3.13. There should be a system to control microbiological contamination in the product before sterilisation.

3.14. There should be no possibility for mix ups between sterilised and non sterilised products. Physical barriers or validated electronic systems may provide such assurance.

3.15. The sterilization records should be checked for compliance to specification by at least two independent systems. These systems may consist of two people or a validated computer system plus a person.

3.16. The following additional items should be confirmed prior to release of each batch of product.

- All planned maintenance and routine checks have been completed in the sterilizer used.
- All repairs and modifications have been approved by the sterility assurance engineer and microbiologist.
- All instrumentation was in calibration.
- The sterilizer had a current validation for the product load processed.

3.17. Once parametric release has been granted, decisions for release or rejection of a batch should be based on the approved specifications. Non-compliance with the specification for parametric release cannot be overruled by a pass of a sterility test.

4. Glossary

Parametric Release

A system of release that gives the assurance that the product is of the intended quality based on information collected during the manufacturing process and on the compliance with specific GMP requirements related to Parametric Release.

Sterility Assurance System

The sum total of the arrangements made to assure the sterility of products. For terminally sterilized products these typically include the following stages:

(a) Product design.
(b) Knowledge of and, if possible, control of the microbiological condition of starting materials and process aids (e.g. gases and lubricants).
(c) Control of the contamination of the process of manufacture to avoid the ingress of microorganisms and their multiplication in the product. This is usually accomplished by cleaning and sanitization of product contact surfaces, prevention of aerial contamination by handling in clean rooms, use of process control time limits and, if applicable, filtration stages.
(d) Prevention of mix up between sterile and non sterile product streams.
(e) Maintenance of product integrity.
(f) The sterilization process.
(g) The totality of the Quality System that contains the Sterility Assurance System e.g. change control, training, written procedures, release checks, planned preventative maintenance, failure mode analysis, prevention of human error, validation calibration, etc.