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Current GMP Guidance / Revision of Annex 15

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Current Validation Guidance

Annex 15 - current version effective since 2001

Principle

"A risk assessment approach should be used to determine the scope and extent of validation"

- Promotes a knowledge based approach

- Allows flexibility based on scientific rationale

- Leveraging of work done prior to the PV study

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Current Validation Guidance

Annex 15, paragraph 25

"…..In theory the number of process runs carried out and observations made should be sufficient to allow the normal extent of variation and trends to be established and to provide sufficient data for evaluation."

- identify sources of variability
- identify control parameters
- generate enough data to show sources of variability are controlled by the process.

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Current Validation Guidance

Chapter 1 – Quality Management

1.4 "Regular periodic or rolling quality reviews..... should be conducted with the objective of **verifying the consistency of the existing process**, the appropriateness of current specifications for both starting materials and finished product to highlight any trends and to identify product and process improvements."

The manufacturer and MAH should evaluate the results and.....an assessment made of whether corrective and preventative action or any revalidation should be undertaken.

Continued Process Verification **???**

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Inspection Experience

Positive Observations

Establishment of "Technical Services" departments

- Process knowledge management

  SMEs involved in :

  -process transfer
  -process validation
  -investigation of process failure
  -statistical process control

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Inspection Experience

Positive Observations

Elements of continuous process verification

- automated continuous monitoring of a CQA to automatically control the process.

e.g. Compaction force control on tablet compression equipment.

Significant data obtained during processing

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Inspection Experience

Annex 15, paragraph 25

"…..In theory the number of process runs carried out and observations made should be sufficient to allow the normal extent of variation and trends to be established and to provide sufficient data for evaluation.

- It is generally considered acceptable that **three consecutive batches**/runs within the finally agreed parameters, would constitute a validation of the process.

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New Guidance

ICH Q8, 9, 10

encourage proactive approach to process understanding from development through the product lifecycle. Greater regulatory flexibility extended where Quality By Design has been successfully implemented.

QWP Guideline on Process Validation (draft)

Annex 15 – to be modified to take these advances into account.

Ph Eur – new monograph for demonstration of unit dose uniformity using large sample sizes e.g. where PAT systems are employed.

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New Guidance

Concept Paper for Revision of Annex 15

- should be published in the coming weeks

- 3 month public consultation

- opportunity to comment on what has been proposed for the revision and anything which may have been missed.

- will include timeframe for revision and description of the anticipated impact of the revision.

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Thanks for your attention

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