EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

25 February 2010
EMA/CHMP/CVMP/QWP/809114/2009
Committee for Medicinal Products for Human Use (CHMP) & Committee for Medicinal Products for Veterinary Use (CVMP)

Concept Paper on the Revision of the Guideline on Process Validation

Agreed by QWP	November 2009
Adoption by CHMP for release for consultation	17 December 2009
Adoption by CVMP for release for consultation	14 January 2010
End of consultation (deadline for comments)	31 May 2010

The proposed guideline will replace the guideline on process validation CPMP/QWP/848/96 and EMEA/CVMP/598/99.

Comments should be provided using this template. The completed comments form should be sent to QWP@ema.europa.eu

Keywords	Process validation, manufacturing, ICH Q8, ICH Q9, ICH Q10

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7418 8416
E-mail info@ema.europa.eu **Website** www.ema.europa.eu

1. Introduction

This concept paper addresses the need to update the guideline on Process Validation[1]. This guideline was originally adopted in February 2001. With the development of new ICH guidelines Q8[2], Q9[3] and Q10[4], this guideline is being reviewed in order to implement the concepts highlighted in the ICH guidelines.

2. Problem statement

The current guideline does not reflect the recent regulatory developments on Process Analytical Technology (PAT), Quality by Design (QbD) and Real-Time Release Testing (RTRT).

3. Discussion (on the problem statement)

The current guideline was developed before the elaboration of the new ICH guidelines Q8 Pharmaceutical Development, Q9 Risk Management and Q10 Quality Systems. With these new guidelines, additional opportunities are available to verify the control of the process by alternative means to the manufacture of traditional process validation batches. The main objective of process validation remains that a process design yields a product meeting its pre-defined quality criteria. ICH Q8, Q9 and Q10 provide a structured way to define product critical quality attributes, design space, the manufacturing process and the control strategy. ICH Q8 refers to an 'enhanced' approach to pharmaceutical development which includes an alternative to the traditional process validation. Continuous process verification [see definition in ICH Q8(R2) glossary] can be utilised in process validation protocols for the initial commercial production and for manufacturing process changes for the continual improvement throughout the remainder of the product lifecycle. In contrast, the current note for guidance on process validation refers only to the more traditional approach of the manufacture of a number of validation batches to confirm that the process is under control. A revision to the note for guidance on process validation will bring it in line with ICH Q8, Q9 and Q10 documents and add the 'enhanced' approach to the current 'traditional' approach. The annexes of the current guideline will be included in the revised guideline. The revised guideline will also clarify to what extent ICH Q8, Q9 and Q10 should be followed when an applicant wishes to use alternative methods of process validation including continuous verification. The FDA guidance on process validation[5] has been recently revised to take into account ICH Q8, Q9 and Q10. The revision to the note for guidance on process validation will provide a more harmonised approach.

4. Recommendation

The Quality Working Party recommends the revision of the Note for Guidance on Process Validation in order to include the concepts defined in ICH Q8, Q9 and Q10 including continuous validation and monitoring.
The revised guideline will not introduce new requirements on medicinal products already authorised and on the market, but it will clarify how companies can take advantage of the new possibilities given when applying enhanced process understanding coupled with risk management tools under an efficient quality management system as described by ICH Q8, Q9 and Q10 guidelines.

5. Proposed timetable

It is anticipated that the draft guideline could be published for 6 months external consultation 9 months after the adoption on the concept paper by CHMP and CVMP (3Q 2010) and that it could be finalised within 6 months after the expiration of the external consultation period (4Q 2011).

6. Resource requirements for preparation

The development of the guideline will be carried out by Quality Working Party, in co-operation with EU/EEA competent authorities the GMDP Inspectors Working Group, the EMEA PAT Team, the Biologics Working Party (BWP), the Immunologicals Working Party (IWP) and the Herbal Medicinal Products Committee (HMPC).

The QWP will appoint a rapporteur among its members who will:

- Lead the discussion at QWP during the development of the guideline
- Prepare the draft guideline
- Review internal comments before the guideline is published for external consultation
- Prepare a new draft for publication
- Review the external comments received after the expiration of the external consultation period is expired
- Prepare the overview of comments
- Prepare a new draft for finalisation
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The guideline will be discussed at QWP and other meetings as necessary (expected 3/4 times) and at QWP/Interested Parties meetings.

CHMP and CVMP will discuss and adopt the concept paper, the draft guideline before external consultation and the finalised guideline before publication. Member States will provide input via their QWP members.

7. Impact assessment (anticipated)

The guidance will clarify requirements for regulators and industry with respect to process validation taking into account the concepts detailed in ICH Q8, Q9 and Q10. Elaboration of the guideline will facilitate different approaches to process validation than currently detailed in the guideline and thus increase flexibility for industry.
No adverse impact on industry with respect to either resources or costs is foreseen.

8. Interested parties

Pharmaceutical Industry, EU/EEA Competent Authorities, GMP/GDP Inspectors Working Group, EMEA PAT Team, BWP, IWP, HMPC.

9. References to literature, guidelines, etc.

1: CPMP / CVMP Note for Guidance on Process Validation (CPMP/QWP/848/96 and EMEA/CVMP/598/99)
2: ICH Q8 (R2) Pharmaceutical Development
3: ICH Q9 Quality Risk Management
4: ICH Q10 Pharmaceutical Quality System
5: FDA Draft Guidance for Industry. Process Validation: General Principles and Practices