European Medicines Agency
Inspections

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COMMITTEE FOR MEDICINAL PRODUCTS FOR HUMAN USE (CHMP)

CONCEPT PAPER ON THE REVISION OF THE GUIDELINE ON PARAMETRIC RELEASE

AGREED BY QWP	October 2008
ADOPTION BY CHMP FOR RELEASE FOR CONSULTATION	November 2008
END OF CONSULTATION (DEADLINE FOR COMMENTS)	February 2009

The proposed guideline will replace the Note for Guidance on Parametric Release[1]

Comments should be provided to QWP@emea.europa.eu

KEYWORDS	*Parametric release, batch release, sterilisation, Process Analytical Technology, Quality by Design, real time release*

[1] CPMP/QWP/3015/99

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1. INTRODUCTION

This concept paper addresses the need to update the CPMP Note for Guidance on Parametric Release[1]. This Guideline was originally adopted in February 2001.

At the time the guideline was developed, the main application area foreseen was the replacement of sterility testing, and this is clearly reflected in the current guideline text. The possibility to apply the same concepts to areas other than sterility was acknowledged and briefly discussed in the guideline.

However, with the development of the new ICH Q8, Q9 and Q10 guidelines, the general ideas in the current parametric release guideline have been further elaborated. It is therefore reasonable to review its content in the light of these new ICH documents and to extend it to aspects other than sterilisation.

2. PROBLEM STATEMENT

The current CPMP Note for Guidance on Parametric Release does not reflect the recent regulatory development on Process Analytical Technology (PAT), Quality by Design (QbD) and Real Time Release (RTR).

3. DISCUSSION (ON THE PROBLEM STATEMENT)

The current Guideline on Parametric Release was developed before the elaboration of the ICH guidelines Q8 Pharmaceutical Development, Q9 Risk Management and Q10 Pharmaceutical Quality Systems. With the adoption of these new ICH guidelines the ideas elaborated in the current text have been taken further and have been given a solid, internationally agreed, basis.

The focus of the current guideline is on the application of parametric release as replacement of routine sterility testing which, at the time of development, was the area where most experience existed. Even if it is clearly stated in the current guideline that the concepts in it can be applied to any stage of manufacture, detailed information is only given on application of parametric release to sterility.

Today, the focus of interest has been broadened. The ideas of Quality by Design and enhanced process understanding together with Process Analytical Technologies as a means to get approval for Real Time Release and to achieve more flexible regulatory approaches has received a lot of attention, both from Industry and from Regulators. A revision the Guideline on Parametric Release will bring it in line with the ICH Q8, Q9 and Q10 documents and clarify to what extent Q8, Q9 and Q10 should be followed when an applicant wishes to introduce replacement of end product testing by other approaches. By elaborating more on examples from process stages other than sterilisation, the revised guideline will also encourage companies to take advantage of these new developments in the area of pharmaceutical development and manufacture.

The revision of the current guideline should also address issues related to the European requirement for reanalysis of batches imported to the European Union from a third country. The incentive of introducing Real Time (Parametric) Release can be foreseen to be limited if reanalysis according to the product specification has to be done anyway after importation to Europe, even when Real Time (Parametric) Release has been authorised in the EU.

In a letter[2] to the EMEA, the European Commission advised that such reanalysis would not be considered a “necessary test or check to ensure quality of a medicinal product” as required by Article 51 (1) b in Directive 2001/83/EC as amended, if Real Time (Parametric) Release has been authorised in the EU. Before this interpretation is applied to aspects other than sterility testing, the requirements for application of Real time Release to such aspects should be revisited, defining specific obligations for the manufacturer, the Marketing Authorisation Holder and for the competent authorities as regards both assessment and inspections, in order to bring them in line with the existing legislation.

4. RECOMMENDATION

The Quality Working Party recommends that the Guideline on Parametric Release is revised, and possibly its name changed, to better reflect the progress made in this area.

The revised guideline should not introduce new requirements on medicinal products already authorised and on the market, but it should clarify how companies can take advantage of the new possibilities given when applying an enhanced process understanding coupled with applying risk management tools under an efficient quality system as described e.g. by the ICH Q8, Q9 and Q10 guidelines.

5. PROPOSED TIMETABLE

It is anticipated that a draft guideline could be available 10 months after adoption of this concept paper. The draft guideline would then be released for 6 months external consultation before its finalisation within another 6 months after the expiration of the public consultation period.

6. RESOURCE REQUIREMENTS FOR PREPARATION

The development of the guideline will be carried out by Quality Working Party, in close co-operation with the GMP/GMDP Inspectors Working Group, the EMEA PAT Team and the Biologics Working Party.

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

- 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.

The guideline will be discussed at QWP and other meetings as necessary (expected 3/4 times) and at QWP/Interested Parties meetings.

A specific drafting group with the participation of the rapporteur and other experts might be set up if considered necessary (expected 1-2 1 day meetings with the participation of 4-5 experts).

7. IMPACT ASSESSMENT (ANTICIPATED)

No adverse impact on industry with respect to either resources or costs is foreseen.

The guidance will clarify requirements for regulators and industry (applicants for Marketing Authorisation and product manufacturers).

Assessment times should be reduced resulting in products reaching the market more quickly. The number of questions during Mutual Recognition, Decentralised and Centralised Procedures should be reduced.

The implementation of Real Time (Parametric) Release should be facilitated as a result of the revision of the current parametric release guideline.

8. INTERESTED PARTIES

Member States National Competent Authorities, EDQM, CHMP, the GMP/GMDP Inspectors Working Group, the EMEA PAT Team and the Biologics Working Party are the main regulatory interested parties.

Pharmaceutical industry associations e.g. EFPIA, EGA, APIC-CEFIC, AEGSP are the main external interested parties.

9. REFERENCES TO LITERATURE, GUIDELINES ETC

1. 'Parametric release' (CPMP/QWP/3015/99)
2. European Commission letter of 2007-05-30 (ENTR/F/2 SA/sp D(2007) 15615)