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Committee for Medicinal Products for Human Use (CHMP)

Concept paper on the need for a guideline on process validation of medicinal products containing biotechnology derived proteins as active substance

DRAFT

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

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1. Introduction

This concept paper addresses the need to develop guidance on process validation of biotechnology derived active substances.

2. Problem statement

Guidelines related to the quality of Biotechnological/Biological products have been developed at the EU level, and several documents have been harmonised through the ICH process. However, these documents do not satisfactorily address the specific aspects of validation and evaluation for biotechnology derived products.

3. Discussion

Validation and evaluation are essential concepts when setting the manufacturing process steps of biotechnology derived products. The evaluation/validation data provide essential information on the reproducibility and robustness of the process steps and are an important element to guarantee consistency in the quality of the product. The data encompass studies that are performed on product and process steps representative of the commercial process and may cover a wide range of situations and experiments (e.g. full scale, pilot scale, laboratory scale, scaled-down), depending on the objectives of the evaluation/validation studies carried out during development (e.g. consistency, viral safety evaluation, process-related impurity clearance).

The currently approved guidelines address the control of Biotechnological/Biological products (i.e. ICH Q6B on specification and ICH Q5C on stability), and/or some specific issues or aspects of the process (i.e. ICH Q5A on viral safety, ICH Q5B on genetic stability, ICH Q5D on cell substrates and ICH Q5E on comparability). ICH Q11, currently under development, is aimed at addressing the description, development, control strategy and process evaluation/validation of active substances of biotechnological and chemical origins. Although ICH Q5 and ICH Q11 documents address several important aspects or concepts relating to the evaluation/validation for medicinal products containing biotechnology derived proteins as active substance, as illustrated above there is no guidance to cover other aspects such as process- and product-related impurity clearance (e.g. host cell proteins, DNA), column/membrane sanitization and life time, hold time, reprocessing, pooling of intermediates and selection of batches to be included in evaluation/validation studies. All these elements do contribute to a good understanding of the process and the resulting product, and are needed for the assessors at the time of evaluation of a marketing authorisation application.

It is well acknowledged that ICH Q8, Q9 and Q10 guidelines are progressively being implemented in the routine practice of manufacturers and marketing authorisation holders. However, whereas these guidelines provide a new approach on the management of quality and build up the quality at every step of the life cycle of a medicinal product, they do not provide practical recommendations on the necessary evaluation/validation studies to be filed on these specific aspects (new application or variations).

4. Recommendation

The Biologics Working Party (BWP) recommends developing a guideline on process evaluation/validation of medicinal products containing biotechnology derived proteins as active substance. This guideline should focus on data requirement for process validation/evaluation for submission of a marketing authorisation application or variation. This guideline will have to take into

account the existing guidances and new concepts and integrate them (by appropriate cross referencing) in the evaluation/validation approach which will be described in the guideline.

5. Proposed timetable

It is anticipated that the draft guideline will be released for consultation in the first quarter of 2012, followed by a 6 month external consultation period prior to finalisation of the document.

6. Resource requirements for preparation

BWP will be responsible for the drafting of this guideline. A drafting group should be formed, which will meet at dedicated drafting group meetings and also in the margin of BWP meetings and via remote conferencing. Where appropriate, a workshop between different stakeholders (assessors and inspectors from national competent authorities, biotech companies…) may be required depending on the comments that will be received following the external consultation.

7. Impact assessment (anticipated)

The guidance will clarify requirements for regulators and industry with respect to process evaluation/validation of medicinal products containing biotechnology derived proteins as active substance.

8. Interested parties

Competent authorities of the Member States and pharmaceutical industry

9. References to literature, guidelines, etc.

ICH Q5A (CPMP/ICH/295/95), Q5B (CPMP/ICH/139/95), Q5C (CPMP/ICH/138/95), Q5D (CPMP/ICH/294/95) and Q5E (CPMP/ICH/5721/03) guidelines

ICH Q6B (CPMP/ICH/365/96) guideline

ICH Q7 (CPMP/ICH/4106/00) guideline

Draft ICH Q11 guideline

CPMP Position Statement on DNA and host cell proteins (HCP) impurities, routine testing versus validation studies (CPMP/BWP/382/97)