European Medicines Agency
Evaluation of Medicines for Human Use

London, 15 December 2004
EMEA/CHMP/BWP/124447/2004

COMMITTEE FOR MEDICINAL PRODUCTS FOR HUMAN USE (CHMP)

CONCEPT PAPER ON THE DEVELOPMENT OF A GUIDELINE ON

VIRAL SAFETY EVALUATION OF BIOTECHNOLOGICAL PRODUCTS TO BE USED IN CLINICAL TRIALS

AGREED BY THE BIOTECHNOLOGY WORKING PARTY	10 November 2004
ADOPTION BY CHMP FOR RELEASE FOR CONSULTATION	15 December 2004
START OF CONSULTATION	20 December 2004
END OF CONSULTATION	21 March 2005

7 Westferry Circus, Canary Wharf, London, E14 4HB, UK
Tel. (44-20) 74 18 84 00 Fax (44-20) 74 18 85 45
E-mail: mail@emea.eu.int http://www.emea.eu.int

CONCEPT PAPER ON THE DEVELOPMENT OF A COMMITTEE FOR MEDICINAL PRODUCTS FOR HUMAN USE (CHMP) GUIDELINE ON

VIRAL SAFETY EVALUATION OF BIOTECHNOLOGICAL PRODUCTS TO BE USED IN CLINICAL TRIALS

Introduction and problem statement

Current guidance on the viral safety of biotechnological medicinal products is found in ICH Q5A - Quality of Biotechnological Products: Virus Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin (CPMP/ICH/295/95 - adopted April 1997). Q5A does not provide guidance for products in development, either prior to or during clinical trials; rather it is directed towards data requirements for marketing authorisation applications.

Clinical trials within the EU are regulated by Directive 2001/20/EC[1]. Approval of trials is the responsibility of individual Member States, who are required to evaluate the products used in clinical studies. Assuring the viral safety of medicinal products of biological origin is a complex process. A reliable assessment of viral safety is critical for weighing the foreseeable risks against the anticipated benefits for trial subjects on which the decision for approving clinical trials is based. The current lack of common reference guidance on which to base the assessment of viral safety of clinical trial material and the difference in experience among sponsors and competent authorities alike, prevents a harmonised approach throughout the European Union and represents a barrier in particular for multi-centre clinical trials. The need for guidance in this area has been recognised by regulators and the Industry[2].

Consequently, it is proposed to develop a new guideline with the title "Viral Safety Evaluation of Biotechnological Products to be used in Clinical Trials".

Discussion and recommendation

Although guidance would be beneficial for various biological products, it is proposed to limit the scope of the guideline initially to biotechnology products in order to provide the most specific guidance possible in this area for regulators and for the Industry. Taking account of existing guidance established for submission of Marketing Authorisation Applications for biotechnology products[3], the proposed guideline would address specific aspects relevant to materials under development.

The guideline would address the following aspects:

1. The extent of viral safety studies, especially validation studies, that are required prior to and during clinical development. For example, investigational products for phase I study are often manufactured at pilot scale, and during development there will be scale-up and other modifications of the manufacturing process. For validation studies prior to a phase I study, there are differing opinions as to how many viruses should be assessed within the validation study and how robust such studies should be, compared with material being used for phase III studies. Validation studies are complex and expensive and a clear position on this is important.

2. The extent to which manufacturers are able to refer to in-house experience concerning virus safety evaluation. For such cases, the virus safety of a given cell culture system and/or the capacity of

[1] Directive 2001/20/EC of the European Parliament and of the Council of 4 April 2001 on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use

[2] The need for guidance in this area was confirmed at the September 2003 joint PDA/EMEA European Virus Safety Forum in Langen (Germany).

[3] ICH Q5A, Note for Guidance on Quality of Biotechnological Products: Viral safety Evaluation of Biotechnology Products derived from Cell Lines of Human or Animal Origin (CPMP/ICH/295/95 - adopted April 1997)

established manufacturing process steps to inactivate/remove potential virus contaminants may have been demonstrated with several previously developed products. Such a database may serve as supportive data to justify a reduced virus safety evaluation program for new products that enter development. Depending on the content of the database the requirements for performing product specific virus safety studies may thus vary. These considerations may not apply for a company developing a product for which they have little prior manufacturing experience.

3. The critieria to take into consideration in the design of preliminary viral safety evaluation studies include:

- the nature of the cell line
- the history of the cell line and its use
- use or non-use of raw materials of human and/or animal origin
- exposure to adventitious contamination
- prior data on viral inactivation/removal steps
- experience of the company with the cell line involved
- experience of the company with specific inactivation/removal procedures to be used
- published data

4. The risk analysis which should form part of the safety evaluation, and the level of requirements with respect to the stage of development and the format of data to be presented.

Timetable and resource requirements for preparation

A drafting group has been formed, which can meet in the margins of the BWP and which will liaise with experts from National Authorities involved in the approval of clinical trials in Member States. It is aimed that a guideline for consultation can be adopted in the second half of 2005 by BWP/CHMP, followed by a 6-month consultation period.

Involvement of external parties

In the preparation of this guideline, the BWP will liaise and exchange experiences with experts from national authorities in charge of approval of clinical trials in Member States.

Impact Assessment

The development of this Guideline is part of the ongoing general development of suitable quality standards. It will result in a more consistent assessment of applications for clinical trials by regulators, set clear standards and expectations for industry, and therefore be helpful in a harmonised regulatory policy.

The relatively small resource implications for preparation of a Guideline are fully justified and are compensated by the fact that application of a Guideline will make assessment easier and will result in less resources being needed during assessment.