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COMMITTEE FOR HUMAN MEDICINAL PRODUCTS (CHMP)

CONCEPT PAPER ON THE REVISION OF THE POINTS TO CONSIDER ON XENOGENEIC CELL THERAPY MEDICINAL PRODUCTS

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AGREED BY BWP	16 May 2007
ADOPTION BY CHMP FOR RELEASE FOR CONSULTATION	22 May 2007
END OF CONSULTATION (DEADLINE FOR COMMENTS)	31 August 2007

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1. INTRODUCTION

Xenogeneic cell therapy is the use of viable animal somatic cell preparations suitably adapted for: (a) the transplantation/ implantation/ infusion into a human recipient or (b) extracorporeal treatment through bringing (non-human) animal cells into contact with human body fluids, tissues or organs. The human use of xenogeneic cells is associated with difficult obstacles, including immunological rejection and management of the risks of transmitting known and unknown pathogens. Importantly, there is the potential risk of introducing new infectious diseases into the general population through adaptation in an immuno-suppressed host. These risks may be minimized – but not completely ruled out - by careful choice of donor animals, reproducible manufacturing process, accurate pre-clinical and clinical testing and monitoring as well as a risk management programme with regard to infectious agents. Therefore, the Points to Consider on Xenogeneic cell therapy medicinal products has been developed in 2002 to provide guidance on the various aspects that might have an impact on the benefit/risk of these products.

2. PROBLEM STATEMENT

Since the publication of the Points to Consider on Xenogeneic cell therapy medicinal products in 2003, research in the areas of xenogeneic cell therapy products and xenotransplantation has moved on. Even though so far no marketing authorisation applications have been submitted for these products, the scientific content of the Points to Consider needs to reflect latest developments.

Also the European pharmaceutical legislation has evolved, providing a clearer legal framework for xenogeneic cell therapy and xeno-transplantation medicinal products. This should be reflected in the revised Point to Consider document. Further legislation, currently under development (i.e. the Regulation on Advanced Therapies), is likely to provide a legal basis for tissue engineered products containing xenogeneic cells.

Last year, Biologics Working Party (BWP) and Working Party on Cell-based products (CPWP) prepare the *Guideline on human cell-based medicinal products* (EMEA/CHMP/410869/2006): this guideline is now published for external consultation. To give clear and consistent guidance, it is proposed to align the Points to Consider on Xenogeneic cell therapy products with the Guideline on human cell-based medicinal products. Thus the revised Points to Consider will focus on issues specific to xenogeneic cell-based products.

3. DISCUSSION (ON THE PROBLEM STATEMENT)

Advanced therapies, including xenogeneic cell therapy is a fast evolving field: both the legal/regulatory framework and scientific development have evolved since the publication of the Points to consider on Xenogeneic cell therapy medicinal products in 2003. Furthermore, the scope of this document should be enlarged to include guidance on xeno-transplantation medicinal products and tissue engineered products containing xenogeneic cells.

4. RECOMMENDATION

The BWP and CPWP recommend to revise the Points to Consider on Xenogeneic cell therapy medicinal products. All parts of the points to consider will be updated if required, but in particular, following sections have been identified for revision:

- The **introduction and scope** will be updated to reflect the changed regulatory and legal situation for these products. Scientific development of xenogeneic cell therapy products and xenotransplantation will be reflected.
- The section on **sourcing of animals** will be revised and updated where needed.
- In the **manufacturing** section, the parts which are common for human and xenogeneic cell-based products will be replaced by a cross-reference to the *Guideline on human cell-based medicinal*

product. Guidance specific for xenogeneic cells, e.g. on organ/tissue and cell manipulation and on screening for infectious agents in the starting material will be updated if needed.

- Many parts of the section on **non-clinical testing** will be replaced by a cross-reference to the *Guideline on human cell-based medicinal product*. The guidance described in the part 'Other toxicity studies' is specific for xenogeneic cells and will be updated and expanded if needed.
- The sections on **human efficacy and safety and on Pharmacovigilance and special surveillance methods** will be brought in line with the *Guideline on human cell-based medicinal product*. The subsections on Registries and Surveillance of close contacts and health care providers will be updated (possible harmonisation with the requirements for human cells and tissues, as inscribed in Directive 2004/23/EC).

In line with the document *Procedures for European Union guidelines and related documents within the pharmaceutical legislative framework* (EMEA/P/24143/2004) and because of the extension of the scope to include guidance on tissue engineered products containing xenogeneic cells, it is proposed to change the title of this document into: 'Guideline on xenogeneic cell-based medicinal products'.

5. PROPOSED TIMETABLE

After adoption of the concept paper, it is anticipated that the draft revised guideline will be adopted and released for 6 months consultation in the first quarter of 2008.

6. RESOURCE REQUIREMENTS FOR PREPARATION

BWP will be responsible for the revision of the section on sourcing of animals and manufacture, CPWP will revise the section on non-clinical and clinical testing and on pharmacovigilance and surveillance. BWP will seek advice, if needed, from veterinary experts (via the CVMP) for the revision of the section on animal sourcing; GTWP will be consulted with regards the part on genetically modified animals; CPWP will consult the Pharmacovigilance Working Party for the section on pharmacovigilance and surveillance.

Initial drafting of the revised sections will be performed independently by BWP and CPWP. Small BWP and CPWP drafting groups might be established to take this drafting forward. It is expected that a joint BWP-CPWP drafting group will be set up to finalise this revision.

7. IMPACT ASSESSMENT (ANTICIPATED)

It is important to keep the guidance up-to-date in a rapidly moving field, such as advanced therapies. Furthermore, harmonisation of requirements for human and xenogeneic cell-based products is also aimed for. It is therefore expected that this revision will contribute to the development of xenogeneic cell-based products and will harmonise the evaluation of these products when submitted for marketing authorisation.

8. INTERESTED PARTIES

Following working parties will be consulted prior to external consultation: SWP, EWP, GTWP, PhVWP and the Committee for Veterinary Medicinal Products (CVMP).

Pharmaceutical industry and academic centres developing xenogeneic cell-based products.
Competent authorities and assessors.

9. REFERENCES TO LITERATURE, GUIDELINES

- Points to consider on xenogeneic cell therapy medicinal products (EMEA/CPMP/1199/02)
- Guideline on human cell-based medicinal products (EMEA/CHMP/410869/2006, draft)
- Part IV of the Annex I to Directive 2001/83/EC as amended
- Procedures for European Union guidelines and related documents within the pharmaceutical legislative framework (EMEA/P/24143/2004)