The European Agency for the Evaluation of Medicinal Products
Evaluation of Medicines for Human Use

London, 16 November 2000
CPMP/BWP/3326/99

CONCEPT PAPER ON THE DEVELOPMENT OF A COMMITTEE FOR PROPRIETARY MEDICINAL PRODUCTS (CPMP) POINTS TO CONSIDER ON XENOGENEIC CELL THERAPY

1. INTRODUCTION

Xenogeneic cell therapy refers to live cells or tissues from a non-human animal source administered to a human recipient. The xenogeneic cell therapy medicinal products - currently under development - can be administered for example by infusion or implantation. The relevance of *ex-vivo* use will be further discussed during the preparation of the Points to consider document.

The definition of a xenogeneic cell medicinal product must be compatible with the definition of human somatic cell product (*Points to consider on Human somatic cell therapy*, in preparation).

Although organ xenotransplants do not fall within the scope of this document however the principles set out in this document may be relevant.

The driving force for the use of xenogeneic cells and tissues is the insufficient supply of human organs/cells. Numerous attempts have been made to implant xenogeneic cells or tissues into patients. In general, these attempts have been unsuccessful, mainly because of immunological incompatibility. Recent advances in protecting xenogeneic cells from immunorejection may reduce the technical hurdles.

From the public health point of view, the risk of cross-species transmission of infectious agents remains the most serious obstacle for the use of living xenogeneic cells in humans.

In the light of Commission communication 98/C 229/3 a xenogeneic cell therapy product can be classified as a medicinal product. The need for guidance by the CPMP for xenogeneic cell therapy products is triggered by some recent developments:

- Manufacturers are already developing xenogeneic cell therapyproducts and the development of a guidance document by the CPMP will contribute to the proper evaluation of risks and benefits connected with their use;
- The draft *Points to consider on Human somatic cell therapy* excludes xenogeneic cells and refers to future specific guidance;
- The draft revised *Note for guidance on Gene transfer* includes only xenogeneic cell lines and also refers to future guidance on special clinical problems in the use of xenogeneic cells.

2. PROBLEM STATEMENT

There are hopes among physicians and patients that the use of xenogeneic cell therapy products will open new therapeutic possibilities. However, the use of xenogeneic cells or tissue involves serious ethical, scientific, public health and other issues.

A critical benefit risk evaluation is warranted for each product and proposed indication, and must take into account both the available therapeutic alternatives for the subject and the potential risks for the whole population.

The creation of this document does not indicate an acceptance of clinical development of xenogeneic cell products, but rather, it should serve as a tool for harmonising the approach to the evaluation of medicinal products containing xenogeneic cells.

The proposed document should be complementary to several existing CPMP guidelines, in particular with:

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- *Note for guidance on the Quality and preclinical aspects of gene transfer medicinal products* (being revised)
- *Points to consider on Human somatic cellular therapy* (in preparation)

The main issues covered by the proposed Points to Consider should include:

- choice of animal species
- animal husbandry
  - selection of donor animals, screening for infectious agents
  - archiving of animal tissue samples
- quality issues in the production process
- requirements for preclinical testing
- requirements for clinical evaluation

need for special clinical safety monitoring, e.g. duration and frequency of monitoring, relevant tests for infectious agents

- public health issues
  - follow up of individuals in close contact with the patient
  - archives for human tissue samples
  - need for special surveillance systems

RECOMMENDATION

It is proposed that a CPMP Points to consider be prepared to address the issues mentioned above by using a multidisciplinary approach, including input from veterinary experts. A need to organise expert meetings dealing with new scientific aspects of xenogeneic cell therapy products is foreseen.

The proposed document would consist of three main sections; the first covering the quality issues (BWP), the second preclinical development (SWP) and the third covering special human clinical safety and efficacy issues (EWP&PhWP).

It is essential that this document is frequently and regularly updated because of rapid technical and scientific advances.

TIMETABLE

A Points to consider should be available for submission to the CPMP at the end of 2001, for release for external consultation.

REFERENCES

1. Commission communication (OJ EC C229/4 of 22.07.98): Commission communication on the Community Marketing authorisation procedure for Medical Products.
2. CPMP Note for Guidance: Gene therapy product quality aspects in the production of vectors and genetically modified somatic cells.
3. FDA Guidance for Industry: Guidance for Human Somatic Cell Therapy and Gene Therapy
4. Federal Register: Draft Public Health Service Guideline on Infectious Disease Issues in Xenotransplantation.
5. Steering Committee on Bioethics (CDBI) European Health Committee (CDSP) Working Party on Xenotransplantation (CDBI/CDSP-XENO (2000) 2 Rev 1): Legal, Regulatory and Scientific Developments in the Field of Xenotransplantation.
6. Concept paper on the Development of a Committee for Proprietary Medicinal Products (CPMP) Points to consider on Human somatic cellular therapy (CPMP/BWP/2257/98 25 February 1999).
7. Concept paper on Xenogenic cell therapy, Report by the Swedish Committee on Xenotransplantation No. 1999:120.