European Medicines Agency
Evaluation of Medicines for Human Use

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CONCEPT PAPER ON THE DEVELOPMENT OF A COMMITTEE FOR MEDICINAL PRODUCTS FOR HUMAN USE (CHMP) GUIDELINE ON NONCLINICAL TESTING FOR INADVERTENT GERMLINE TRANSMISSION OF GENE TRANSFER VECTORS

Introduction

The possibility of exposure of gonadal tissue to gene transfer medicinal products raises safety concerns about vertical germline transmission of vector DNA. While inadvertent germline transmission has not been observed in clinical trials to date, recent findings of vector DNA in semen of clinical trial participants have renewed concern. With new technologies allowing more advanced and effective *in vivo* gene therapy strategies, the risk of inadvertent germline transmission might increase accordingly.

Problem Statement

The need for nonclinical germline transmission testing to support clinical development of gene transfer medicinal products has recently been subject to discussions of the CHMP in relation to several scientific advice requests.

The issue of nonclinical testing for germline transmission is mentioned in the current Note for Guidance on the quality, preclinical and clinical aspects of gene transfer medicinal products (CPMP/BWP/3088/99). However, at the present stage of gene therapy research, an updated and more detailed guidance on the extent of nonclinical testing is warranted.

Discussion

The guideline should provide an updated evaluation of the type and extent of nonclinical studies needed to investigate the potential for inadvertent germline transmission in support of the clinical development of new gene transfer medicinal products.

The extent of nonclinical studies needed to adequately investigate the possibility of inadvertent germline transmission will depend on varying parameters such as vector type, route of administration and disease targeted. These aspects will be addressed in the guideline.

Recommendation

The guideline will complement the current Note for Guidance on gene transfer medicinal products (CPMP/BWP/3088/99). The CHMP Gene Therapy Expert Group (GTEG) has produced a scientific report on the issue of inadvertent germline transmission, and this report will be used as background information for the development of the guideline. The CHMP GTEG will continue to be consulted during the preparation of this CHMP SWP guideline.

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Timetable

The draft concept paper will be forwarded to the CHMP for adoption in November 2004. A draft guideline is expected to be forwarded to CHMP for release for consultation in May 2005.

Resource requirements for preparation

The CHMP GTEG will be consulted during the preparation of this CHMP SWP guideline.

Impact assessment

The development of this Guideline is part of the ongoing general development of suitable guidance for medicinal gene therapy products. It will result in a more consistent assessment of applications for non-clinical data of gene therapy products by regulators, set clear standards and expectations for industry, and therefore be helpful in a harmonised regulatory policy.