CONCEPT PAPER ON THE DEVELOPMENT OF A COMMITTEE FOR MEDICINAL PRODUCTS FOR HUMAN USE (CHMP) GUIDELINE FOR THE NON-CLINICAL DEVELOPMENT OF FIXED COMBINATIONS OF MEDICINAL PRODUCTS

Introduction

Several diseases are being treated with multiple medicinal products with complementary actions. There are also situations where one medicinal product is combined with another in order to improve its efficacy and/or safety. The concomitant use of medicinal products may trigger the development of a fixed combination product.

Problem statement

At present, there is limited regulatory guidance within the EU for the non-clinical studies that are recommended to support the development of a fixed combination product. In the Note for Guidance CPMP/EWP/240/95, there is a general paragraph about non-clinical studies and other guidance documents refer to general factors of concern for fixed combination products. However, there is no clear / detailed guidance on the non-clinical development of a fixed combination medicinal product. The need for guidance is reflected in the many Scientific Advices requested since 1995.

Recommendation

The main aim of the non-clinical studies to support development of a fixed combination is to characterise potential additive, synergistic, potentiation or antagonistic effects of the compounds when used together, and thus to obtain information on expected as well as potential unexpected interactions and to characterise both the pharmacology, pharmacokinetics and toxicology of the combination under development. Several different scenarios for a fixed combination exist. For instance, there may be a fixed combination of compounds already approved to be used in combination, a combination of two well known/approved compounds not approved for use in combination, a combination of a new chemical entity (NCE) with an approved/well known compound, or the combination of two NCEs.

The Guideline should give guidance to industry about the non-clinical strategies to be considered when developing a fixed combination based on the different data available in order to support the safe human use as well as avoid unnecessary repetition of animal studies.

Timetable

Draft Guideline to be finalised in December 2004 at the Safety Working Party and presented to CPMP in January 2005 for discussion and release for consultation.