European Medicines Agency

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COMMITTEE FOR MEDICINAL PRODUCTS FOR HUMAN USE (CHMP)

CONCEPT PAPER ON THE DEVELOPMENT OF A CHMP GUIDELINE ON EXTRAPOLATION RESULTS IN CLINICAL STUDIES TO THE EU-POPULATION

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1. INTRODUCTION

Up to a few years ago, clinical data used to come from trials conducted in the US, EU and places like Canada, South Africa or Australia. Recently this has changed however, with trials being conducted in other countries or even worldwide. As such this is not an issue, but the relevance of the data for the EU patients is not always clear and extrapolation sometimes doubtful. Moreover, there are also examples of results of trials, conducted globally, for which the interpretation of the data for EU was difficult.

The reasons for differences may vary, but these products present difficulties for interpreting the data for EU patients.

2. PROBLEM STATEMENT

In ICH E5 the possible influence of ethnic factors on results and the interpretation of results is discussed. A distinction is made between intrinsic and extrinsic factors. Though intrinsic factors exist, it is clear from the examples that extrinsic factors are more troublesome and their effect is less well understood and sometimes not taken into account during drug development. This results in large trials being conducted with less or no value for the EU.

To prevent a situation where this is seen at filing, a reflection paper might be needed to highlight the issue to industry and regulators.

3. DISCUSSION (ON THE PROBLEM STATEMENT)

To get more understanding of the issue and the possible extrinsic factors of importance for a discussion on relevance of data for the EU a background research in a number of files, including the examples mentioned in the Introduction might be useful.

Based on that a reflection paper could be drafted, emphasising ICH E5 where relevant.

The discussion should also be extended to situations where problems might be foreseen, e.g., neonatal studies and studies in children in general.

To prevent a situation of studies being conducted which cannot be used for filing in the EU, it should be discussed how this issue can be put in the Scientific Advice in a more systematic way.

For harmonisation assessors should pay attention to this issue in a systematic way and it should be investigated whether the AR template could be updated for this purpose.

The usefulness of a workshop could also be addressed.

4. RECOMMENDATION

A reflection paper should be developed by the EWP, taking into account the above-mentioned discussion points.

5. PROPOSED TIMETABLE

Before that a background research in a specified number of files is needed. This will take 2 months. A draft reflection paper is foreseen in July 2007.

6. RESOURCE REQUIREMENTS FOR PREPARATION

The Rapporteur is responsible for the background research. The draft will be finalised in the EWP, after discussion in the cardiovascular drafting group. Two (2) meetings are anticipated.

7. IMPACT ASSESSMENT (ANTICIPATED)

The Reflection Paper will help in emphasizing the need for companies to think the issue through before trials are started and in harmonisation and consistency of assessments.

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