European Medicines Agency

London, 22 February 2007
Doc. Ref. EMEA/CHMP/EWP/44238/2007

COMMITTEE FOR MEDICINAL PRODUCTS FOR HUMAN USE (CHMP)

RECOMMENDATION ON THE NEED FOR REVISION OF (CHMP) POINTS TO CONSIDER ON THE REQUIREMENTS FOR CLINICAL DOCUMENTATION FOR ORALLY INHALED PRODUCTS (OIP) (CPMP/EWP/4151/00)

AGREED BY THE EFFICACY WORKING PARTY	January 2007
ADOPTION BY CHMP FOR RELEASE FOR CONSULTATION	22 February 2007
END OF CONSULTATION (DEADLINE FOR COMMENTS)	31 May 2007

Comments should be provided to Line.Jensen@emea.europa.eu
Fax +44 20 7418 86 13

KEYWORDS	*Orally inhaled products, guidance*

7 Westferry Circus, Canary Wharf, London, E14 4HB, UK
Tel. (44-20) 74 18 84 00 Fax (44-20)
E-mail: mail@emea.europa.eu http://www.emea.europa.eu

1. INTRODUCTION

This PtC document is intended to complement the guideline on pharmaceutical documentation of inhalation products. It has to be seen as an additional framework to the existing guidance.

2. PROBLEM STATEMENT

The effect of an inhaled product is brought about by a complex mechanism involving not only the active substance itself, but also its formulation, the inhalation device and the interaction of the patient with the device. Therefore, demonstration of therapeutic equivalence (TE) between two inhaled products is generally more difficult compared to conventional dosage forms, such as tablets.

This guideline was created as a link to other existing guidelines (e.g. guideline on replacement of CFCs) and mainly focuses on TE. Taking into account that the guideline on CFCs will phase out in the near future, due to finalisation of CFC replacement, it seems necessary to transfer some main issues concerning TE into the PtC on OIPs.

In addition, the guideline on CFCs only covers TE as a part of propellant replacement in pressurised metered dose inhalers (pMDIs); issues pertaining to dry powder inhalers and non-pressurized MDIs fall outside its scope. Therefore an extension and modification for these kinds of products should also be considered.

Finally, recent application procedures revealed a need for a change of policy: it is necessary to guide applicants on how to proof TE with a convincing assay sensitivity to claim a hybrid application with inhalation products.

3. DISCUSSION

Following issues should be considered when updating the guideline:

1. The CFC guidance on TE is of limited relevance due to its narrow scope (only applies to a change in propellant in pMDIs).
2. The PtC contains partial guidance on the issues of TE, but also refers to the CFC guidance which will be of little relevance within a few years. The reference in the PtC to the CFC guidance should be removed.
3. Design recommendations in the current guidance are insufficient and contradictory:
    - The study duration stated in the two documents is contradictive.
    - The requirements for demonstration of TE should be more detailed. There is now evidence that some designs used in the past for demonstration of TE lacked assay sensitivity, but were compliant with current guidance. New guidance should contain specific recommendations for demonstrating assay sensitivity. Moreover, in situations where multiple indications are sought, the guidance should contain recommendations for these situations.
    - More specific recommendations should be considered in relation to different drug classes (e.g. a distinction between short- and long-acting $beta_2$ agonists, inhaled corticosteroids, anticholinergics) and combination products.
    - Recommendations are necessary for products, where the dose strengths of the reference product are non-linear.
4. There is a need for updating the requirements in relation to the use of spacers in specific populations. For example, a named spacer should be used in the clinical studies in accordance with the guideline on pharmaceutical documentation of inhalation products.
5. The title should reflect the main issues of the guideline (i.e. considering a restriction of the guideline for hybrid applications of OIPs in the treatment of asthma and COPD).

6. The PtC should clearly distinguish between requests for hybrid applications, variations and line extensions.

4. RECOMMENDATION

It is proposed to revise the CHMP-Guideline < **Points to consider on the requirements for clinical documentation for orally inhaled products (OIP)** > **CPMP/EWP/4151/00** to provide an updated EU consensual regulatory point of view on the above-mentioned issues.

5. TIMETABLE

It is anticipated that a draft revised CHMP guideline will be available 6 months after adoption of the recommendation document for 6/3-months released for external consultation, before finalisation within 6 months.