European Medicines Agency

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COMMITTEE FOR MEDICINAL PRODUCTS FOR HUMAN USE (CHMP)

CONCEPT PAPER ON THE NEED FOR REVISION OF THE NOTE FOR GUIDANCE ON PHOTOSAFETY TESTING (CPMP/SWP/398/01)

AGREED BY SWP	06 December 2007
ADOPTION BY CHMP FOR RELEASE FOR CONSULTATION	24 January 2008
END OF CONSULTATION (DEADLINE FOR COMMENTS)	31 May 2008

The proposed guideline will replace the Note for Guidance on Photosafety Testing CPMP/SWP/398/01.

Comments should be provided using this template to SWP Secretariat: EMEA-H.SWP@emea.europa.eu

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KEYWORDS	Phototoxicity, photoirritation, photoallergy, photogenotoxicity, photocarcinogenicity, non-clinical, UV absorption, *in vitro* models

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1. INTRODUCTION

The goal of photosafety testing is to detect the adverse effects of pharmaceutical products in the presence of light. This type of testing is relevant for medicinal products that enter the skin via dermal penetration or systemic circulation. Photobiological reactions normally occur when a chemical is able to absorb UV or visible light. A Note for Guidance (NfG)[1] on photosafety testing was adopted by CPMP in June 2002 and came into operation in December 2002. The key objectives of this document is to define criteria when photosafety testing is needed and to provide guidance on how to evaluate non-clinically the different possible endpoints of adverse photo-reactions, i.e. phototoxicity (photoirritation), photoallergy, photogenotoxicity and photocarcinogenicity.

2. PROBLEM STATEMENT

Accumulating data and experiences with regulatory photosafety testing over the past years have revealed some shortcomings of the current guideline recommendations that was adopted in 2002. New data and developments in the field are now available that would better define guidance for photosafety testing.

3. DISCUSSION

The following points have been identified as critical issues of the current guideline that need an update in order to improve the recommendations for the evaluation process of photosafety of pharmaceuticals:
(1) The criteria for deciding whether photosafety testing is needed are rather non-specific and apparently result in testing of too many new pharmaceuticals. A refinement of the criteria to allow a better prediction of possible photobiological properties or lack thereof is required.

(2) If testing of a product is considered necessary the guideline stipulates a parallel approach with different tests covering the endpoints phototoxicity, photoallergy, and photogenotoxicity. A tiered approach, where photoallergy and photogenotoxicity testing would usually not be required if the compound in question is clearly negative in an initial in vitro phototoxicity study would provide a more suitable and efficient testing strategy.

(3) Oversensitivity and the occurrence of “pseudo-effects” with *in vitro* models recommended by the current guideline, in particular the mammalian cell test for photo-genotoxicity have become a major problem. Therefore the use of these test models for regulatory purposes can no longer be justified and need to be replaced by more appropriate approaches.

(4) The current guideline does not address the question of the timing of photosafety evaluation during drug development. In order to avoid uncertainty in this respect some guidance should be provided.

4. RECOMMENDATION

The CHMP SWP recommend to revise the existing guideline on photosafety testing in order to overcome the identified shortcomings, taking into account the experiences with regulatory photosafety testing over the past years and new developments in the field.

5. PROPOSED TIMETABLE

It is anticipated that a draft of a revised Guideline may be available 9 months after adoption of the Concept Paper. The draft Guideline will be released for 6 months for external consultation.

6. RESOURCE REQUIREMENTS FOR PREPARATION

The preparation of this Guideline will only involve the SWP.

7. IMPACT ASSESSMENT

The development of a revised Guideline is anticipated to render more precisely the conditions when performance of photosafety testing is required and thus avoid unnecessary testing and to provide clear recommendations for an efficient and reliable evaluation of pharmaceuticals for potential adverse photo-reactions.

8. INTERESTED PARTIES

The pharmaceutical Industry and individual National Competent Authorities involved in safety assessment of pharmaceuticals.

9. REFERENCES

Note for Guidance on Photosafety Testing (CPMP/SWP/398/01).