The European Agency for the Evaluation of Medicinal Products
Evaluation of Medicines for Human Use

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AD HOC WORKING GROUP ON HERBAL MEDICINAL PRODUCTS

Final Comments for Revision of Notice to Applicants Volume 2A Part 1.4.2 – Bibliographical Applications

RELEASE FOR CONSULTATION BY THE EMEA	January 1998
DEADLINE FOR COMMENTS	April 1998
RELEASE OF FINAL PROPOSALS	September 1998

Note:

Modifications from the original texts proposed by the group are in *bold italic.*

The views presented in this document are those of the HMPWP, which has been created as a forum for exchange of experience in the field of herbal medicinal products. This document is released for the purposes of transparency and has no legal force with respect to Directive 2001/83/EC.

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Final comments for revision of Notice to Applicants Volume 2A Part 1.4.2
Bibliographical applications

The working group suggests including a paragraph on scientific monographs into the Notice to Applicants Volume 2A
In Chapter I – 'Marketing Authorisations'
Section 4 – 'Stand Alone Applications for a Marketing Authorisation'.

4.2 BIBLIOGRAPHICAL APPLICATIONS

1. Where the constituent or constituents of the medicinal product have a well established medicinal use, with recognised efficacy and an acceptable level of safety, demonstrated by detailed references to published literature presented in accordance with second paragraph of Article 1 of Directive 75/318/EEC, an application (so called "bibliographical") for marketing authorisation may be submitted in accordance with Directive 65/65/EEC, article 4.8.(a)ii.

2. An applicant wishing to use Article 4.8 (a)ii) of Directive 65/65/EEC must fully satisfy all the requirements of Article 1 of Directive 75/318/EEC as well as those of Directives 65/65/EEC and 75/319/EEC as amended, in effect, submit a "complete" application.

3. Directive 75/318/EEC Article 1 states that "where pursuant to point 8(a) of Article 4, second paragraph, of Directive 65/65/EEC, references to published data are submitted, the provisions of this Directive (i.e. Directive 75/318/EEC) shall apply in like manner." In such cases, the full article or reference should be supplied, with necessary translations. Moreover, the Expert Reports must clearly state the grounds for using published references under the conditions set out in Directive 75/318/EEC. This would include the completion of all of the tabular formats provided in "The rules governing medicinal products in the European Union, Volume 2B Notice to Applicants: Presentation and content of applications' where relevant, unless there is a justification that the study is no relevant for the medicinal product. The impurity/related substances profile and the decomposition products arising during storage must be clearly indicated in order to allow assessment of appropriate efficacy and safety.

4. In the event that neither detailed reference to published literature, nor appropriate justification is available to cover all the requirements, the applicant must supplement the missing data with appropriate additional studies.

Scientific monographs on certain substances (e.g. those drafted by the European Scientific Co-operative on Phytotherapy (ESCOP) and the World Health Organisation (WHO) for herbal drugs) offer a valuable and updated overview on published scientific literature, which together may be used in support of the demonstration of the safety and efficacy of a medicinal product in a bibliographical application in accordance with Article 4.8 (a)ii. These monographs may help to avoid duplication of work and bring about gradual harmonisation in the evaluation of medicinal products, e.g. herbal medicinal products. Therefore the Commission and Member States recommend that both applicants and competent authorities should make use of these monographs. The use of these monographs should not preclude the future development or implementation of results of new clinical trials.

5. It should be noted that summary assessment reports such as the EPAR for Community marketing authorisations or evaluation reports on Maximum Residue Limits which are made publicly available by competent authorities for reasons of transparency would generally not be considered to supply sufficient information to meet the requirements of Directive 75/318/EEC.