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

Executive Summary

Herbal medicinal products are available in all Member States of the European Union. Industrially prepared, finished herbal medicinal products fall within the scope of Council Directive 65/65/EEC. They have access to the decentralised procedure. Major differences in the assessment of Quality, Safety and Efficacy would hinder free circulation of herbal medicinal products in the EU and may represent a risk for consumers. The complexity of herbal drug preparations and the interpretation of bibliographic data on safety and efficacy, that reflect the experience gathered during long-term use, are addressed best by involving specific expertise and experience.

Upon the initiative of the European Commission and the EMEA Executive Director and with the support of the EMEA Management Board, an Ad Hoc Working Group on Herbal Medicinal Products has been created at the EMEA in May 1997. Members of the group were appointed by the Member States permanent representations to the European Union. Representatives of the European Parliament, the European Commission and the European Pharmacopoeia, who also contributed actively to this activity, demonstrate the high public interest in the subject. The group met for three meetings in 1997.

Over its three meetings this year and in accordance with its mandate defined last June by the EMEA Management Board, the group reviewed the criteria set out in Council Directives for the demonstration of pharmaceutical quality, pre-clinical safety, and clinical efficacy in the case of marketing authorisation applications for herbal medicinal products. The group reviewed the appropriateness of the Notice to Applicants Vol 2A and 2B for herbal medicinal products. The role of scientific monographs prepared by ESCOP and WHO was also discussed.

In the field of quality, the group agreed on a terminology for herbal medicinal products and reviewed existing guidance for Good Manufacturing Practice (GMP), which was considered acceptable. Minor modifications would suffice for updating Annex 7 'Manufacture of Herbal Medicinal Products' of GMP for medicinal products. Concerning documentation on pharmaceutical quality existing guidance is appropriate at present, although modifications would be necessary, in particular to the Note for Guidance "Quality of Herbal Remedies". Taking into account potential difficulties for the testing of complex mixtures, development of further guidance should be considered. The group proposed modifications to the Notice to Applicants 2B, Part II, to better adapt it to herbal medicinal products.

Guidance regarding requirements for non-clinical testing of herbal drug preparations was derived from available draft guidance on requirements for old substances with long term marketing experience. The proposed guidance takes into account experience available in humans for well-established herbal drug preparations.

Although efficacy was recognised as being the most difficult issue, the group agreed on some general principles and reached agreement on a first draft of a core SPC for *Valerianae radix*. The group considered that the drafting of such core SPCs would be the most appropriate way

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to develop general guidance on criteria to assess efficacy data based on bibliographical documentation. The assessment of bibliographic data on efficacy needs further discussion in future meetings.

The role of monographs prepared by ESCOP and WHO was discussed. The group proposed to include a paragraph on scientific monographs into the NTA, Chapter I, Marketing Authorisations, Section 4.2 Bibliographic Applications.

ESCOP made a presentation to the working group on their study on the pharmacovigilance of herbal medicinal products. The group acknowledged the effort made by ESCOP to collect clinical safety data for herbal drugs. These data could be useful in future discussions on core-SPCs. Because herbal medicinal products are subject to pharmacovigilance regulations as set out by Directives any interference with these systems in force has to be avoided.

The subjects discussed by the working group were presented to Interested Parties who unanimously supported the continuation of this work beyond 1997. Industry confirmed their willingness to co-operate in encouraging new research in the field of clinical pharmacology and clinical efficacy in order to obtain modern clinical data on herbal medicinal products. They also expressed a great interest in commenting on all proposals for revision of documents prepared by the working group. These proposals will be released by the EMEA Secretariat for consideration by Interested Parties including learned societies.

All members of the group found the outcome of the three meetings extremely useful for developing common criteria for the assessment of herbal medicinal products and promoting mutual recognition of marketing authorisations. The assessment of bibliographic data on efficacy needs careful consideration. A continuation of work was proposed.

The European Commission and the Pharmaceutical Committee expressed their great satisfaction with the creation of the group and the progress achieved within a short time. A continuation of the work was strongly suggested.

Proposals for future work include discussion and implementation of comments presented by Interested Parties and scientific organisations on the proposals prepared in 1997, preparing additional and more detailed guidance for the pharmaceutical documentation, establishment of listings of herbal drugs available in the Member States, discussion of scientific monographs and preparation of core SPCs, drafting a Points to consider document on criteria to assess efficacy of herbal medicinal products on the basis of bibliographic data and preparing criteria for the assessment of fixed combinations of herbal drug preparations.

A full report was presented to the EMEA and European Commission. The EMEA circulated the report to the CPMP and to the Mutual Recognition Facilitation Group.

The mandate of the Ad Hoc Working Group on Herbal Medicinal Products and the press releases of the three meetings held in 1997 are available upon request from the EMEA Secretariat.