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Evaluation of Medicines for Human Use

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**HMPC WORKING PARTY ON
COMMUNITY MONOGRAPHS AND COMMUNITY LIST (MLWP)**

Hearing AESPG – 10 March 2009
Report

List of AESGP representatives
Christelle Anquez-Traxler, Werner Busse, Valerio Bombardelli, Frans van den Dungen, Florence Guillaume, Marie-Laure Lacoste, Mónica Mennet-von Eiff, Barbara Steinhoff, Marinella Trovato.

The MLWP Chair welcomed the representatives from AESGP and Dr Busse expressed thanks for the opportunity to raise issues related to the preparation of Community herbal monographs and Community list entries directly with the MLWP. AESGP welcomes the work of the MLWP and recent initiatives for a pragmatic approach to the development of monographs and list entries. Considering the challenging environment faced by companies, Dr Busse reminded all participants that a market-oriented approach is of benefit for European patients and consumers. It would indeed be better to regulate plants having medicinal properties in humans as medicinal products rather than as dietary supplements. There are however many requirements associated with the status as medicinal product (e.g. GMP, Pharmacovigilance). Monographs represent a great opportunity to market products as medicinal products if monographs' indications are useable in a marketing scenario.

1. AESPG remarked on the **difficulty for the HMPC to grant well-established medicinal use indication** to several plants despite the fact that literature references was provided which AESGP believes meet the criteria of the HMPC guideline on the assessment of clinical safety and efficacy.

The HMPC Chair pointed to the different documents where the reasoning of HMPC decisions can be found. Controversial assessment often lead to the adoption of monographs and list entries by majority votes and divergent positions by committee members are appended to the published HMPC opinion. The rationale for acceptance/rejection of comments received during public consultation is found in overviews of comments which complement the assessment reports (AR). Finally, minutes from MLWP meetings can be accessed in accordance with EMEA Rules for the implementation of Regulation (EC) No 1049/2001 on access to EMEA documents.
These documents should help interested parties to understand why some studies are not found appropriate to support a well-established use indication. The referred guideline points to the need for one controlled clinical study of good quality, which shall be consistent with and be assessed together with a broad range of documented evidence.
The HMPC Chair remarked that, where the committee has failed to be transparent on its assessment of some literature references, it shall issue a corrigendum. This will be the case for Harpagophyti radix as the conclusions on the assessment of a number of clinical studies will be added to the published AR. AESGP was thanked for this example of good cooperation with the HMPC.

The HMPC Chair recognised that there are critical cases where there is controversy over the results of clinical studies considered pivotal and they deserve particular attention. Having regard to its rules of procedure, the HMPC is willing to consider the opportunity for hearings in connection with controversial scientific evaluations. The committee would be particularly keen to meet experts from the concerned clinical field, with a preference for those having been involved in the conduct of the relevant clinical study. Such hearings should be limited to borderline cases: they would provide a

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chance for the HMPC to debate controversial views when positive results must be balanced against methodological deficiencies.

2. AESGP would appreciate the **simultaneous publication of draft assessment reports and draft monographs** as a routine procedure as it would facilitate the preparation of comments.

The MLWP Chair explained that it is difficult for the MLWP to commit to always release both documents at the same time. They are progressed in parallel but not entirely to the same extent at the same time. Due to the complex process of preparation of AR, serious delays with the release of draft monographs would occur if the draft AR was to be published simultaneously. The MLWP Chair was however confident that the positive experience with Hyperici herba would be repeated in the future for particular complex assessments.

3. AESGP made a plea to really **secure a 3-month public consultation period**.

The MLWP Chair reaffirmed the MLWP/HMPC willingness that 3 full months are available for interested parties to comment on draft monographs and list entries, as well as on any draft guidelines or other guidance documents.

4. AESGP enquired about possibilities for a **fast identification of final versus draft monographs** on the EMEA website.

Although the MLWP Chair pointed out that this is not a priority for the MLWP/HMPC, she indicated that the HMPC secretariat would look into this matter.

5. AESGP sought for an update on the **list entries which are not finalised because of lacking genotoxicity data**.

The HMPC Chair actually returned the question to AESGP, enquiring whether it had heard from its members about efforts to gather genotoxicity data in a coordinated way. B. Steinhoff reported about ongoing initiatives in Germany. The performance of experiments is however distinct from the submission of tests results to health authorities. The latter indeed remains entirely a choice of the companies. The HMPC Chair remarked that access to unpublished genotoxicity data is a crucial element for the HMPC to progress with the establishment of the list of herbal substances, preparations and combinations thereof for use in traditional herbal medicinal products. He urged AESGP to invite companies to submit such unpublished data to the EMEA where they would be used for the sole purpose of establishing Community list entries. AESGP confirmed that they would take the message home to their member companies. However, the ultimate decision to share its own data lies with the company.

6. AESGP enquired about **access to MLWP tracking system for assessment work** so as to allow seeing the **development status of monographs** beyond the foreseen timelines in the MLWP work programme.

The HMPC Chair explained that the MLWP does not yet operate with the support of electronic tools but rather upon the manual maintenance of internal lists. The meeting report is an important tool of communication where reference to “significant progress” indicates the forthcoming release of final monographs and related documents.
The MLWP Chair added that MLWP members had discussed releasing timetables for the preparation of monographs/list entries, practice had however shown that they are not reliable due to unforeseen delays or fast progress.

7. AESGP enquired about the existence of concrete plans for **cooperation with EFSA**. AESGP was particularly keen to hear about cooperation as regards health claims for herbal ingredients.

The HMPC Chair reminded participants that, despite the coexistence of distinct legislation in the food and pharmaceutical areas, specific provisions of European legislation, in particular Regulation (EC) No 726/2004, point to the need for European bodies to identify potential sources of conflict between their respective scientific opinions and act together to resolve such conflicts. Cooperation with EFSA on health claims and therapeutic indications for herbal ingredients is encouraged, the modalities of which are yet to be discussed. Although it is not possible to intervene in the work carried out by EFSA at present and by DG SANCO in the future, it would be difficult to justify to the general public that two bodies could come to divergent conclusions upon assessment of the same clinical data and using similar assessment criteria.
He finally added that Dr J. Koch is the official observer from the HMPC to the EFSA Scientific Cooperation Working Group on Botanicals (announced in the May 2008 HMPC meeting report) and that Professor Vlietinck brings in his experience as a MLWP member and as an alternate HMPC member.

8. AESGP enquired about the close **cooperation between the HMPC and the EDQM**, asking if there is a joint working programme or a list of priority items planned to be jointly tackled by both parties.

The MLWP Chair explained the recent initiatives taken to strengthen coordination between HMPC and EDQM. Beyond the mutual appointment of observers (HMPC observers have recently been appointed to EDQM Groups of Experts in Phytochemistry 13A and 13B), the MLWP Chair monitors newly published volumes of Pharmeuropa. Finally dedicated meetings with the Chairs of the EDQM Groups on Experts in Phytochemistry and TCM will be held on an annual basis. The Quality DG Chair added that an action plan has been established which include limits for quantified extracts, distinction between active markers and analytical markers, choice of most relevant assays for marker substances, etc. He did also participate in the EDQM 'Steering Committee for the procedure for the certification of suitability to monographs of the European Pharmacopoeia'. It was remarked that 2 applications for certification of suitability had been received in 2008 for herbal medicinal products.
B. Steinhoff expressed appreciation of these developments and she reiterated a plea for harmonisation of terminology with a view to abolishing discrepancies in terms in particular between herbal substances & herbal drugs and herbal preparations & herbal drug preparations.

9. AESGP comments on the draft 'Concept paper on the preparation of a guideline on the **preparation of herbal teas**' (EMEA/HMPC/451978/2008)
The HMPC Chair reported the surprise of the MLWP/HMPC vis-à-vis the comments raised on this concept paper and the conclusions to a misunderstanding of the HMPC's intention. Rather than to address industrial production, the MLWP aims to establish instructions for end-users on the preparation of herbal teas so that individual monographs could refer to such a general paper.
B. Steinhoff clarified that the release of a guideline could lead to a standardisation of herbal teas and such overregulation appeared inappropriate given that compliance to current requirements ensures that herbal teas are safe.
The HMPC Chair remarked that, in the framework of Mutual Recognition/Decentralised Procedures, the existence of a European understanding of terms such as 'infusion', 'maceration' and 'decoction' is desirable, given that these terms are not yet defined in the Eur. Ph. Hence, the document would be a explanatory / glossary document, rather than a guideline.

10. Prospect with **use of MRP and DCP provisions**

AESGP reported a more positive outlook by companies on the perspective to use MRP and DCP provisions than that presented in 2008 (see report from AESGP hearing in May 2008). The release of major monographs such as the monograph on Hyperici herba is an important element in companies' strategies for European market access. The HMPC Chair again invited companies to seize existing

opportunities: for example he pointed to the list entries on sweet fennel fruit and on bitter fennel fruit and their indication for the symptomatic treatment of minor spasm associated with menstruation period.

Finally AESGP was invited to inform the HMPC on the organisation's views on what should the HMPC priority activities be for the next couple of years.

AESGP invited all HMPC members to a conference on herbal (medicinal) products and food supplements to be held on 6-7 October 2009 in Brussels. Once final the program will be sent to all HMPC members.
On behalf of AESGP, Dr Busse thanked MLWP members for the constructive dialogue and looked forward to a continued cooperation. The MLWP Chair thanked AESPG representatives for the fruitful discussion and closed the hearing.