EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Patient Health Protection

Hearing AESGP during MLWP May 2010 meeting

Report

List of Association of the European Self-Medication Industry (AESGP) representatives
Christelle Anquez-Traxler, Valerio Bombardelli, Werner Busse, Hubertus Cranz, Nand De Herdt, Marie-Laure Lacoste, Monica Mennet-von Eiff, Tinne Pletinckx, Olivier Ricq, Bernd Roether, Barbara Steinhoff

The Chair of the Working Party on Community Monographs and Community List (MLWP) welcomed the representatives from AESGP and Dr Cranz expressed thanks for the opportunity to discuss a number of issues related to the establishment of Community herbal monographs and Community list entries as well as general matters relevant to other tasks incumbent to the Committee on Herbal Medicinal Products (HMPC). Dr Busse introduced the 'AESGP position paper on the experience with the EU legislation on traditional herbal medicines' which had been prepared as a result of the invitation to AESGP, during the hearing[1] held in March 2009, to present the organisation's views on what should be the HMPC priority activities for 2010-2011. Dr Steinhoff, Dr Busse, Dr Cranz and Dr Anquez-Traxler took turn in introducing the various topics for discussion.

1. AESGP reported on experiences by companies in the assessment of applications as part of the national implementation of Directive 2004/24/EC in the Member States. Beyond concerns about the level of fees for traditional use registration in some countries, those related to deviations from monographs and substantial delay in some assessment procedures call into question the validity of the simplified scheme. Industry is hoping for an improvement of the situation in the year to come. The HMPC Chair wondered whether the release by AESGP of some relative performance indicators would be beneficial for identifying the reasons of such delays.

2. AESGP expressed satisfaction vis-à-vis positive changes in relation to the quality of guidelines and Community monographs and the functioning of the MLWP. AESGP welcomed the recent cases of **release of draft monographs for public consultation together with the supporting assessment reports**. The MLWP Chair announced a change in the policy of the working party after Rapporteurs highlighted the increased quality of the comments raised by interested parties in relation to a greater understanding of the data assessed and of the preliminary conclusions reached. Assessment reports will continue to be released with a disclaimer pointing to their nature as 'working document, not yet fully edited' and the MLWP will retain the discretion not to publish a draft

[1] http://www.ema.europa.eu/pdfs/human/hmpc/18044209en.pdf

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assessment report, if concurring with the views of the Rapporteur and Peer-reviewer that the document has not reached a sufficiently advanced stage of preparation to be released.

3. AESGP asked for information, including rational and likely timeline, on the announced class-review for plants used in BPH (e.g. Serenoae repentis fructus, Cucurbitae semen) in relation to the assessment of Urticae radix put on hold in January 2010. The MLWP Chair made the link to the assessment work on Oleae folium put on hold in March 2010 for the same reason. A legal interpretation is needed concerning the provisions in Article 16a(1)(a) of Directive 2004/24/EC relating to **indications appropriate to traditional herbal medicinal products**. There may be a situation whereby patients, after a first diagnosis by a medical doctor, are aware of the condition they suffer from and as such they may be in a position to consider the use of a traditional herbal medicinal product as part of the management of their condition. The HMPC Chair commented on the various aspects to be considered in the legal analysis, such as the level of evidence that support the therapeutic indications. The place of herbal medicines within the category of non-prescription drugs was emphasised. Besides the legal aspect of the question, AESGP pointed to the societal dimension of 'self-medication' and to its evolution over the last 20 years. The notion of 'collaborative care[2]', whereby patients treat or prevent short term or chronic illnesses after an initial medical diagnosis, is now well-accepted.

4. AESGP enquired about the project to develop a reflection paper addressing the necessity of initiatives to stimulate the conduct of **clinical studies with herbal medicines in the paediatric population**. The paediatricians in the MLWP pointed to the different aspects of the problem, from the lack of incentives for companies to carry out expensive controlled clinical trials, the legal restrictions in accepting clinical experience as a valuable source of evidence, to the difficulties of conducting observational studies in this population. The HMPC Chair referred to expected coordination with the CMD*h* with a view to accessing data on paediatric studies with HMP which are due for assessment by the Agency/CMD*h* Subgroup[3] Paediatric Regulation. However, considering the anticipated timelines of the work-sharing approach for the assessment of these data, industry is invited to reflect on a two-step approach whereby, first, list of paediatric studies would be made available to the HMPC, followed, upon request, by the submission of literature and studies. As regards the above-mentioned reflection paper, coordination with the PDCO is being sought prior to the release for public consultation. Dr Busse pointed to the costs range of the investment represented by the conduct of such clinical studies which can only be compensated by adequate duration of data exclusivity.

5. AESGP made a proposal for the development of Community monographs on well-known **combinations** whereby herbal substances and/or preparations could be combined as long as with the same or very similar indication(s), in analogy to the approach taken in the past in the French Avis aux fabricants and German Commission E monographs; both documents could be used to provide the history of medicinal use in Europe. The HMPC Chair remarked that the transposition of those systems is not simple and would require the introduction of a matrix model with minimum and maximum posology for the various components. He added that the HMPC has no capacity to analyse combination products available on the market and identify the priority combinations to be assessed. Furthermore, one MLWP member remarked that more information is needed concerning the proposed 'conditions' for acceptance of combinations. AESGP agreed to reflect on the questions put forward: would the plant's constituents profile be considered beyond the proposed 'same indication' criteria? what would be the maximum number of preparations in the combination? are combinations welcome in all therapeutic areas? The HMPC Chair suggested a future dedicated discussion of 5 to 10 concrete examples. AESGP concurred to the need for further feasibility investigation.

[2] http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=COM:2008:0666:FIN:en:PDF
[3] http://www.hma.eu/272.html

6. In order to make the implementation of the Directive 2004/24/EC even more transparent, AESGP asked if the overview of MA and registrations granted per Member State (ref. EMEA/HMPC/148505/07) published on the Agency website could be updated at regular intervals. AESGP suggested including in the overview of granted registrations/authorisations the name of the product, the herbal substance, preparation or combination thereof used, and the therapeutic indication(s) granted. The HMPC secretariat indicated that a centralised reporting on the **uptake of the simplified TU registration procedure** is one the objectives set in the 'Action plan for herbal medicines 2010-2011' referred to in the last HMPC meeting report. Completion of this objective will however be dependent on the cooperation of the national competent authorities in providing via the CMD*h* the data on a regular basis.

7. Acknowledging that the current legislative framework would need to be modified, AESGP pointed to some future directions to be understood in the context of current challenges faced by companies in their applications for market access. As previously mentioned, timelines in excess of 3 years for the evaluation of applications, levels of application fees and deviation from monographs' content justify industry's proposal that the HMPC should become the sole scientific committee with responsibilities for herbal medicines including a **centralised registration/authorisation** associated to a reasonable fee structure. The political nature of the proposal was acknowledged and the MLWP as a scientific group could not comment.

8. Provisions regarding **referrals to the HMPC** were raised. It was acknowledged that provisions of Article 30 of the Community code (so-called 'divergent decision' referrals) do not apply to traditional use registrations. Again, a modification of the legislation is needed to provide applicants with the possibility to trigger a referral to the HMPC in the context of a purely national evaluation, on condition that the request for an HMPC opinion is properly motivated.

9. AESGP asked for an update on the on-going **dialogue between the HMPC/MLWP and EFSA**, especially in light of the recent developments on health claims. The HMPC Chair commented on the few meetings which took place between representatives of EFSA, in particular its NDA Panel, and the Agency. The MLWP/HMPC note published EFSA/NDA opinions with great interest and that the NDA approach appears to be transparent and consistent. The HMPC Chair indicated that EFSA did not yet contact the Agency/HMPC for exchange of information and dialogue about a botanical and related health claim(s) (within the scope of the agreed cooperation between both agencies to avoid potential conflicting opinions).

10. AESGP commented on the Agency decision that **divergent positions appended to HMPC opinions** on Community herbal monographs cannot be released under the Agency Rules[4] for the implementation of Regulation (EC) No 1049/2001 on access to European Medicines Agency documents. These divergent positions come under the system of exceptions set out in the implementing rules whereby 'access to a document containing opinions for internal use as part of deliberations and preliminary consultations within the Agency shall be refused even after the decision has been taken if disclosure of the document would seriously undermine the Agency's decision-making process'. The HMPC Chair concurred with AESGP view that such information is critical for companies seeking to market in Europe herbal medicinal products containing preparations covered by a Community herbal monograph. He promised seeking discussion of the current policy within the Agency, having considered the grounds for refusing access and the reasons why access to the name of the HMPC members who have expressed the divergent positions appended to HMPC opinions on monographs should be granted.

[4] http://www.ema.europa.eu/pdfs/general/manage/mbar/20335906en.pdf

11. AESGP enquired about the 'Exchange on Information on herbal medicines' as an output of the **Transatlantic Administrative Simplification Initiative** reflected in the action plan between the Agency and the U.S. FDA. The HMPC secretariat confirmed the transmission of final monographs on 2 occasions in 2009 via the European Commission and reported on the forthcoming 3rd transmission directly to the FDA, in coordination with the Agency International Liaison Officer. No feedback was received from the FDA so far. AESGP reported on debates in the U.S. on the dietary supplements legislation and encouraged the Agency to continue sharing with the FDA the European scientific monographs which the HMPC can be proud of.

12. AESGP was informed about the tools in place for a successful dialogue and **cooperation with EDQM** whereby the expertise in both fora are confronted to ascertain the selection of the best possible specifications and requirements in herbal monographs of the European Pharmacopoeia.

13. AESGP was informed about the intended new consultation of interested parties for the **prioritisation** of pending assessment works and the identification of new herbal substances, preparations and combinations thereof for assessment. AESGP was invited to take part in the exercise which shall be announced in the meeting report from the May HMPC meeting.

Dr Cranz thanked the MLWP Chair, HMPC Chair, MLWP members and HMPC secretariat for the fruitful discussion. The MLWP Chair thanked AESGP representatives for the constructive dialogue. The HMPC Chair concluded on the usefulness of such hearing that shall be repeated again.

Upcoming conferences organised by AESGP were highlighted, which allow debates on developments in the field of OTC, Food Supplements and/or Herbal Medicinal Products.