EUROPEAN MEDICINES AGENCY
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Patient Health Protection

Hearing AESGP during May 2011 MLWP meeting

Report

List of Association of the European Self-Medication Industry (AESGP) representatives

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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 and the national registration of traditional herbal medicinal products.

1. Dr Anquez-Traxler gave a presentation on the outcome of a **survey** amongst companies operating in the sector of herbal medicines, on their experience with the evaluation of their marketing authorisation/registration application. The survey had been conducted as a result of the discussion held, during the AESGP hearing in May 2010, on costs, delays and deviation from Community herbal monographs in the assessment of herbal medicinal products' applications. Data thus were collected in particular on requested fees, timelines for the review, use of monographs, number and nature of questions raised during the evaluation, level of accessibility of the authorities before and during the procedure. A total of 124 questionnaires completed between September and December 2010 had been analysed and this figure was put in perspective against the ≈360 traditional use registrations (TUR) which had been granted by the EU Member States and the ≈ 900 TUR applications under assessment by the end of December 2010 (1).

The HMPC Chair confirmed the imminent publication by the Agency secretariat of the data obtained from the Member States on TUR, as the first step in the objective laid down in the 'Action plan for herbal medicines 2010-2011' (2) to report regularly on the uptake of the simplified procedure set out in Directive 2004/24/EC and on the marketing authorisation of herbal medicinal products. Publication will take place at both the EMA and Heads of Medicines Agencies websites.

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The results of AESGP's survey were overall positive, yet providing some hints on areas for improvement for a regulatory environment in competition with other legal frameworks and therefore scrutinised for its constraints, which, if they become too cumbersome, would be detrimental for the sector.

Openness and accessibility of the authorities were scored positively in the majority of the Member States and the specific expertise in herbal medicines for assessors would contribute to improve the review procedures in place. Shorter review timelines and proportionate fees were advocated, and in that context, the acceptance and respect of monographs established by the HMPC is a drive for fast procedures and reduced costs. Amongst the 124 procedures surveyed, a monograph had been used in 42% and the summary of product characteristics granted was in line with the monograph in the majority of cases.

Within Europe's aim for better regulation, too restrictive recommendations or new requirements represent hurdles for the regulation of herbal medicines and AESGP conveyed the wish for pragmatism during companies & authorities' dialogue.

It was noted that all 124 procedures in the survey were national procedures and the reasons for the still very limited use of DCP/MRP by companies were not investigated in this survey. The content and full acceptance of adopted HMPC monographs are thought to be key factors in the decision by companies to use these procedures for their marketing strategies.

2. This led AESGP to move on commenting on the **general functioning** of the HMPC and MLWP in the establishment of monographs and Community list entries. The functioning of the MLWP is found satisfactory by AESGP which endeavours to provide sound and quality comments on draft monographs released for public consultation. Key to the recognition of herbal medicines in the scientific community, AESGP considers that studies of good quality when they are present should lead to the acceptance of 'well-established' use in HMPC monographs. The Chair of the MLWP remarked that the working party sometimes needs several rounds of discussion to discern the scientific opinion that all or a majority of members can endorse, when the relevance and/or quality of studies are disputed. Formal adoption takes place in the Committee where members can express a divergent position, made public on the EMA website as an appendix to the document where the HMPC opinion, reached by consensus or a majority vote, is recorded. A greater transparency on this adoption process may be considered, in the future, in the Committee meeting reports where the adoption of draft and final monographs is announced. A trend towards more and more adoptions by consensus is a positive sign of greater harmonisation in this field across the Member States.

3. Upon AESGP's query on **procedural steps** for recent cases where substantial changes occurred between the draft and the final versions of a monograph, the HMPC Chair commented on the pressure that had arisen from the 30 April 2011 deadline and the Committee's efforts to issue as many monographs as possible in that context. It was clarified that corrigenda to monographs are exceptional and the two corrigenda for the monograph on *Cimicifuga racemosa* allowed the HMPC to remove inconsistencies between the monograph and the assessment report (AR) that were identified after the publication of the monograph which occurred before that of the AR.

The HMPC Chair pointed to the HMPC and MLWP joint aim to reduce the time for publication of documents once adopted by the Committee. Reference was made to the communication on this matter in the HMPC public meeting report from March (3).

Current case where draft assessment reports have not yet been published during the public consultation on draft monographs that will end on 15 June was raised. It was confirmed that the new policy foresees the release of both a monograph and its supporting assessment report at the same time. Where the release of the AR is delayed, it is acknowledged that interested parties have less time

than anticipated until the deadline to comment on the draft monograph. The reasons for such delay may be specific, in any case AESGP was reassured that every effort is made to adhere to intended process and timelines, considering available resources at the time. An extension of the deadline for comments may be considered.

4. Concerning the **prioritisation of assessment works**, AESGP was thanked for responding to the invitation in 2010 for interested parties to express their views on the priority level of a number of pending assessment works. The MLWP Chair confirmed that the proposal by AESGP for new assessment works had found a positive echo amongst the members, as Rapporteurs could be identified and the 3 herbal substances Andrographidis paniculatae folium, Capsici fructus and Erysimi officinalis flos had consequently been added to the priority list (4) and a call for submission of scientific data published respectively[1]. All levels of priority assigned by AESGP in September 2010 appear in column C of the inventory (5). Rapporteurs will take these levels into consideration within each of their individual work plans. The HMPC Chair remarked that the complexity of an assessment work because of high volume of literature is a factor affecting the timelines of preparation of a draft assessment report and monograph, and for major plants, the interests of patients and those of all other stakeholders in getting scientific recommendations at European level are considered when deciding on priorities.

5. AESGP expressed its position concerning the **proof of tradition**. Such a proof might consist in an individual proof of a product which has been on the market for 30 years or longer (including at least 15 years within the European Union), or within a description of a preparation in the literature. In AESGP's point of view, it should be sufficient if the use of the preparation (normally going back for some decades) is described in the literature, e.g. in older textbooks or pharmacopoeia monographs but the book itself does not need to be 30 years old. The MLWP Chair responded that the working party has been rather strict in applying the legislative requirement for 30-year evidence of medicinal use during monographs' establishment. When evidence amounted to only 26 or 27 years, some preparations were not included in a monograph, considering that these preparations could in any case be registered on a national level upon submission of a dossier by an applicant, outside the framework offered by the monographs. The HMPC Chair added that the provisions of Directive 2001/83/EC amended by the Directive 2004/24/EC represent already an important derogation from the need to submit results from safety and efficacy tests and trials. The HMPC therefore has taken the approach that evidence of a regular use for 30 years is necessary to be convinced that no safety risk had emerged from real use during such a period. Information from textbooks is important, however it cannot substitute entirely for the range of data and documentation that the HMPC considers necessary to accept a traditional use.

6. The question of the use by the HMPC/MLWP of **data not in the public domain** for the establishment of monographs was raised. Dr Cranz indicated that data submitted by AESGP as part of their comments on draft monographs can be used unless they are marked as confidential. Data protection and data confidentiality are being discussed by the EMA in the context of the establishment of a given monograph. There was agreement that, unless a company has given explicit permission to use unpublished data in support of a monograph, they cannot be used by the working party. Dr Cranz acknowledged that a system based on monographs leads to a market made more easily accessible for competitors and this is the known price to be paid for a market access made simpler by the use of such monographs. It is therefore the choice of individual companies to allow the MLWP or not to access data they have generated. Dr Steinhoff reiterated the fact that data included in traditional use registration dossiers assessed by national competent authorities cannot be shared with the HMPC for

[1] http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/document_listing/document_listing_000214.jsp&murl=menus/regulations/regulations.jsp&mid=WC0b01ac0580033a9c

the sake of establishing a monograph. AESGP can always be contacted for clarification on data submitted by the organisation in support of their comments and this should preferably be channelled via the HMPC secretariat. The MLWP Chair suggested that direct contacts between Rapporteurs and any of the parties commenting on draft monographs should be avoided.

7. The organisation of such AESGP hearing in the spring on an annual basis was confirmed as best suited from the point of view of both AESGP and MLWP. The HMPC Chair anticipated that the hearing scheduled for May 2012 will be an opportunity to review the outcome of changes being introduced in the work flow and methodology applied by the HMPC and its subgroups. Dr Cranz appreciated the **constructive dialogue** which aims to build an ever more efficient system where patients, healthcare professionals, regulators and industry work towards a strong European phytotherapy that broadens consumer choice for adequately labelled, safe products and reflects different cultural preferences found in the EU.

The hearing was closed and all participants thanked for the fruitful exchange.

(1) Uptake of the traditional use registration scheme in the EU Member States – Status: 31 December 2010 (EMA/322570/2011)

(2) Action plan for herbal medicines 2010-2011 (EMA/831327/2009)

(3) Meeting report – 40th HMPC meeting held on 30-31 March 21011 (EMA/HMPC/288516/2011)

(4) HMPC overview of assessment work – Priority list (status May 2011) (EMA/HMPC/278067/2006)

(5) Inventory of herbal substances for assessment – May 2011 (EMA/HMPC/494079/2007)