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Committee on Herbal Medicinal Products (HMPC)

AESGP hearing at MLWP meeting, September 2018

Report

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

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AESGP presented a comprehensive overview of the recent assessment of data collected and research update concerning **pyrrolizidine alkaloids (PA)** contamination of herbal medicinal products. From the data collection over the past five years, it can be concluded that a limit of 1.0 µg PA per day in the final product can be kept by most of the herbal drugs and extracts, a reduction to 0.35 µg per day, however, is not feasible. Based on this and a new reference value published by the EFSA Panel on Contaminants in the Food Chain (CONTAM) in a statement 'Risks for human health related to the presence of pyrrolizidine alkaloids in honey, tea, herbal infusions and food supplements' from June 2017, it was advocated that the transitional threshold of 1.0 µg PA per day should become the permanent one. AESGP highlighted the urgency of the issue given companies need early guidance as on how to prepare for the future. The MLWP thanked for the presentation of recent data and showed interest in receiving them in writing. MLWP members acknowledged the fact that it was a high priority and reassured industry that the Working Party and the HMPC were looking into revising the public statement. In this context, AESGP highlighted the status of research projects, particularly those focusing on toxicology, and the promising outcome of the recent workshop in Kaiserslautern focusing on the different PA potencies as important contributions to the ongoing discussion. The activities of the European Pharmacopoeia in the development of a framework for an analytical method were mentioned as well.

The concept of **combination monographs** was welcomed by industry which is looking forward to seeing the ones on Species amarae, Species digestivae and Species sedativae. The MLWP informed that they would indeed be released soon for comments and underlined that the plants can be combined provided they fulfil the traditional use as a combination as laid down in the legislation. In practice, authorities endeavour to be flexible in accepting 'new combinations' whilst complying with the legislation. Analogy was made by the industry to the fixed combination guideline and the fact that justification for a combination was possible (and fewer regulatory requirements applied) if the two

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compounds were used concomitantly in the same disease treatment for example although not combined within one product. If this concomitant use in the same course of treatment can be documented, industry was of the view that it could also help justify the traditional use of a combination of plants.

An exchange of views took place on the status of the **HMPC statement on estragole**. The HMPC and SWP worked together on this issue and the HMPC is now actively updating its statement. It was clear that a substantial lowering of the threshold would put fennel-based products at risk. The MLWP reassured industry that in case of substantial change to the statement, a new consultation would anyhow be organised.

AESGP asked about the follow-up to the HMPC **Reflection Paper on polycyclic aromatic hydrocarbons (PAH)**; the issue is also addressed in the draft revision of the guideline on specifications recently released by the HMPC. Industry offered to contribute to the ongoing discussion by providing data and elements from analysis of PAH in herbal drugs and extracts. It occurs that PAH comes from the environment where it is ubiquitously present, and it can be shown that the vast majority of herbal drugs and extracts are clearly below the level permitted for food supplements. Differentiation needs to be made between PAH arising during the manufacturing process (e.g. from roasting or drying) and the environmental exposure that cannot be avoided. The situation for most extracts is different as PAH is not water soluble and can therefore not be found in aqueous extracts. The MLWP welcomed the submission of data on PAH findings for the re-discussion of the Reflection Paper scheduled for 2019.

The 'Concept paper on the development of a **reflection paper on new analytical methods/technologies** in the quality control of herbal medicinal products' gave rise to a debate as to the objective of such a reflection paper. Further to the comments received from industry, the MLWP clarified that in view of scientific/technological developments the concept paper sought cooperation with interested parties. Providing examples and comments regarding new methods/technologies used in quality control of herbal substances/preparations would help to develop a reflection paper (not a guideline!) to stimulate and foster the dialogue on the subject. It is seen as a regulatory reaction to new opportunities from analytical innovation already available and used. Industry expressed concerns that the document may lead to expectations that those methods need to be used in replacement of the ones currently used in routine quality control. MLWP clarified that any future guidance to industry and authorities should not impose additional requirements but be beneficial for the introduction of new methods complementary to conventional ones if useful. The intended document would provide basic reflections on benefits/limits or also validation. The HMPC has prolonged the deadline for comments to allow collaboration with the intention to move the document further.

Turning to next steps and the impact of the **relocation of the Agency** and the business continuity plan, the industry was informed that the Committee and its subgroups are also affected by temporary scaling back of some EMA activities currently scheduled to last until 30 June 2019. It affects guideline development as well as suspended subgroup meetings (including MLWP). In contrast, HMPC meetings are planned to continue and also prolonged apart from the March 2019 meeting that will be cancelled. However, industry was reassured that work on safety-relevant PA and estragole guidance will continue during that period. Industry expressed sympathy for the difficult situation and recognised that flexibility was needed for the time being until the EMA settles in Amsterdam. The MLWP underlined that it was also looking into its strategy and processes in order to improve efficiency in its work and reflecting on the future of herbal medicines, also looking at more joint collaboration with universities and authorities across the world. It welcomed AESGP's suggestions on future strategic priorities for herbal medicines in Europe.

AESGP thanked for the fruitful and open exchange of views and looks forward to the next exchange in 2019.