



Quality Standards for Herbal Products in Europe – a Report from the Athens Natural Products Conference, August 2008

by Dr. Mathias Schmidt (ANME e.V.)

Organized by the GA (Society for Medicinal Plant and Natural Product Research) in cooperation with the AFERP (Association Francophone pour l'Enseignement et la Recherche en Pharmacognosie), the ASP (American Society of Pharmacognosy), the PSE (Phytochemical Society of Europe), and the SIF (Società Italiana di Fitochimica), the world's most important conference on medicinal plant research took place in Athen from August 3-8, 2008. More than 1,100 scientific contributions from over 70 countries reflect the growing interest in herbal medicinal products.

Traditionally, a workshop on regulatory affairs is held at this conference. Prof. Arnold Vlietinck, who is actively involved in the EMEA's committees for herbal medicinal products and pharmacopoeial monographs, gave a plenary lecture and made an important contribution to the workshop by explaining the current situation of herbal medicinal product registration in the context of dietary supplements – products under food status which may contain exactly the same extracts as herbal medicinal products under drug status.

Whereas the marketing of food supplements only requires a notification of the authorities, drug registration is still more complicated. Whereas there are different categories of HMP (full registration, well-established use and traditional use) which require different amounts of clinical and non-clinical documentation, the requirements for quality are more or less the same for all types of drug registration. Among other factors, they involve production according to GMP (Good Manufacturing Practise) standards, the validation of analytical procedures, respecting pharmacopoeial standards and EMEA recommendations.

To facilitate HMP registration, the EMEA prepares monographs for herbal drugs and preparations. To date, 166 monographs on herbal drugs have been published by the EMEA, 38 drafts are currently under study. In addition, 77 published monographs cover preparations. Still, there is a long way to go until a major part of the medicinal plants and preparations will be covered by EMEA monographs. Even then, an EMEA monograph only has the status of a recommendation.

A major obstacle for transferring a dietary supplement into a drug is clearly the high standards of analytical data. The plant material has to be identified by macroscopic and microscopic examinations as well as by specific assays, and potential contaminants have to be excluded (e.g., heavy metals, pesticides, herbicides, aflatoxins) – examinations, which have to be repeated on the level of the drug product.

One of the most costly and most difficult factors (next to validation of analytical methods) is the requirement for stability data. Stability data is usually measured by long-term testing and by accelerated testing under stress conditions (elevated relative humidity and temperature). Even though the regulations allow for extrapolations of measurements to the double of the *de facto* covered time span (example: 12 months covered, 24 months extrapolated), such an extrapolation is only possible when the accelerated testing does not show any degradation – which will probably rather be an exception than a rule for herbal medicinal products. The latter fact was, however, not discussed by Vlietinck.

To date, dietary supplements do not need to provide data on any of these quality standards. With the current developments in the EFSA, especially the presentation of the Botanical Safety Guideline, things will most probably start to change. Vlietinck pointed to the fact that the very same preparation can either be marketed as a drug – with full documentation of quality –, or as under food status with practically no documentation of quality. He called for bringing quality standards of food supplements and herbal medicinal products to a common level, however, without lowering the standards for herbal medicinal products.

The propositions of Prof. Vlietinck will have to be seen in the general context. Already, such considerations seem to be avidly accepted by the EFSA. Producers of food supplements will consequently have to prepare for much higher quality standards, which will probably mainly economically damage the small and medium size enterprises, but neither the internet trading with completely uncontrolled quality, nor “Big Food”. It may be speculated that such a development is not exactly unwanted by the big players in the food sector – anyway, it will increase the financial burden of small companies producing food supplements.

One conspiracy theory must, however, be discarded: the driving force behind these changes is surely not “Big pharma”. Medicinal products from the sector of complementary and alternative medicine (CAM) are mostly provided by small to medium size enterprises (so-called SME’s), and these companies also suffer from the ever increasing financial burdens regarding toxicology and quality. Especially the highly individualized treatments from Traditional Chinese Medicine or Ayurveda risk to be lost to CAM, as the financial load share for the individual preparation mostly by far exceeds the turnovers.

One of the clearest messages from today’s discussions is: We are living in a time of change, and nobody is able to predict how the legislation will develop – especially with the background of the most recent decisions of European court indirectly calling for more common sense.