



Discussion Paper on “Botanicals and Botanical Preparations widely used as food supplements and related products: Coherent and Comprehensive Risk Assessment and Consumer Information Approaches”

(adopted by written procedure on 23 June 2004)

1. In view of the fact that botanicals and botanical preparations intended for human consumption as food supplements and related products are very widely marketed with a variety of claims, the present discussion paper aims at increasing awareness of some key issues to improve comprehensiveness and coherence of current approaches to risk assessment and consumer information on these products *.
2. A large number of botanical materials (e.g. whole, fragmented or cut plants, algae, fungi, lichens), and botanical preparations obtained from these materials by various processes (e.g. extraction, distillation, purification, concentration and fermentation) readily find their way onto the food supplements market. These materials are also often labelled as natural foods, largely organic, and foods specifically intended to support sport activities. Personal care products and the so-called “traditional herbal medicinal products” represent additional sources of exposure of consumers to botanical products. New products are also emerging, consisting of substances that commonly occur at low levels in botanical components of the diet, which are then extracted and re-introduced at much higher levels in specific products.
3. Botanicals and botanical preparations are widely available to consumers through several distribution channels in the E.U. and elsewhere. In particular, they are sold over the counter in pharmacies and can be bought in supermarkets, herbalist’s shops and other shops, or via the Internet. They are currently available and used in such a way that they are almost becoming part of the common diet, thus providing for a significant human exposure from a public health point of view.

* The use of botanicals and botanical preparations intended for animal consumption is not dealt with in this paper.

4. There are some general concerns with respect to botanicals and botanical preparations mainly relating to quality and safety issues:

- Contamination (both chemical and microbiological) is a documented problem. It has been associated, for example, with botanical products originating from Asia. Deaths through poisoning following consumption of such products have been reported in Europe and the US arising from contamination with heavy metals, synthetic drugs and other undesirable substances (Ernst, 2002). Misidentification of plants harvested from the wild is also a continuing problem. When sales of traditional herbal products remained restricted to particular ethnic groups, which are familiar with the products and able to exert a local control on quality, problems were more rarely encountered. The growing volume of sales in the European Union with products obtained from suppliers based in Asia or elsewhere and the move towards widespread outlets for the products of traditional medicine call for more formal pre-marketing assessment and more stringent controls than the occasional random checks and analyses often carried out by individual national or local authorities on what is already out in the market.
- There is world-wide recognition of potential problems associated with botanicals and botanical products, not only in terms of safety, but also in terms of the claimed amounts and stability of the active ingredients. For example, the US Pharmacopeia, which considers the safety of food supplements as well as medicines, announced in December 2002 the establishment of an advisory panel specifically to advise on improving the quality of botanical products.
- Any efficacy shown by botanical products is usually a product of one or more plant secondary metabolites. Secondary metabolism responds to stress imposed by biotic and abiotic factors and, as a consequence, patterns and concentrations of metabolites can show considerable variation among plants belonging to the same species and variety. For instance, it is not unusual for metabolites produced in response to pathogen attack to vary in concentration one thousand-fold over short time periods. While consistency of product is more easily controlled in cultivated plants, particularly those grown in containment, collections from the wild make it difficult to ensure that concentrations of bioactive agents meet specifications and are within safe limits.
- A very large literature exists on toxic substances naturally-occurring in plants. Of particular concern are plant products consumed in concentrated forms. Concerns can relate directly to the toxicological profile of the active agent(s). It has been the case with kava-kava (*Piper methysticum*), its withdrawal from the market being advised recently because of the association of its consumption

with acute liver failure (Kraft *et al.*, 2001). In June 2001, the US FDA, following action by the UK and Australia, advised manufacturers of dietary supplements to avoid the use of the various types of comfrey (*Symphytum* spp.) because of the health concerns associated with the presence of pyrrolizidine alkaloids. Moreover, since 1993, cases of nephrotoxicity and carcinogenicity have been reported in Belgium, France and United Kingdom as a result of inadvertent exposure to *Aristolochia* species in unlicensed herbal medicines (EMEA, 2000).

- Interactions of herbal products with prescription products are well recognised, although widely under-reported (Ernst, 2000; Sorensen, 2002). In the past, when such products were usually obtained from outlets run by knowledgeable individuals, advice on use and contra-indications was often available. Currently, contra-indications do not usually appear on the labels or any associated documentation when herbal products are sold through supermarkets and other retail outlets. Yet, a survey of the available information on interactions with medicinal compounds of the more commonly purchased botanical products (e.g. ginkgo, garlic, St. John's Wort and ginseng) found recorded adverse interactions for all but *Echinacea* and saw palmetto (Izzo and Ernst, 2001). Incidence and severity of effects associated with prescription drug-dietary supplement interactions in a small group of primary care patients have also been investigated by Peng *et al.* (2004); the most common botanical products included garlic, ginkgo biloba, saw palmetto and ginseng. While most interactions were judged not to be serious, an incidence of 6% of potentially severe health consequences was recorded among patients taking at the same time specific drugs and specific botanical products.
5. This heterogeneous group of commodities includes products which, mainly depending on their intended uses and presentations, fall under different Community regulatory frameworks and for some types of products legal provisions for a preliminary risk assessment do not exist yet. The main legislations to be considered in this context are Directive 2002/46/EC on food supplements and Directive 2004/27/EC on traditional herbal medicinal products:
- Directive 2002/46/EC foresees the use as food supplements of vitamins and minerals listed in the Annexes to the Directive. It also allows the use for the same purpose of still undetermined substances with a nutritional or physiological effect, but definition of such effects is not provided for. According to Art. 4, para 8, the European Commission shall produce, not later than 12 July 2007, a report on the advisability of establishing specific rules, including, where appropriate, categories of additional vitamins and minerals or of substances with a nutritional or physiological effect, accompanied by any

proposals for amendments to Directive 2002/46/EC^{**}. Thus a regulatory framework for further developments in this area already exists.

- Directive 2004/27/EC on “traditional herbal medicinal products” provides for definitions of (i) traditional herbal medicinal products, (ii) herbal medicinal products, (iii) herbal preparations and (iv) herbal substances. The directive introduces a simplified registration procedure, based on “traditional use”, but ensuring quality and safety as for any other medicinal product. Community lists will have to be prepared of traditional herbal medicinal products, herbal preparations and herbal products. On the other hand, traditional herbal materials, which are authorised for use in medicinal products, will continue to contribute to the dietary intake of bioactive agents as long as they comply with the general food regulations and make no medicinal claim.
6. Also relevant in this context are the Directives 1989/398/EEC and 96/84/EC on “Food for special purposes” and the Regulation 1997/258/CE on “novel foods” that provide additional channels for some botanicals and botanical preparations to enter the food market, and the proposed Directives on “nutritional and health claims” and “food fortification” at present under consideration by the European Parliament and Council.
 7. As the market volume expands, so does the need for a better characterisation of botanicals and botanical preparations, and for harmonising the scientific assessment of risks from exposure of consumers to these products.
 8. It is important, therefore, from a public health point of view, to achieve a comprehensive and coherent approach to risk assessment and consumer information on botanicals and botanical preparations widely present in different categories of commodities. Such an approach would, in time, overcome the existing information gaps on many of these products and bring together the fragmentary provisions for risk assessment on botanicals and botanical preparations in the current relevant regulations. To this end, the present paper aims at increasing awareness on these issues and at facilitating a critical analysis of the present situation. It is intended to lead to a stronger partnership and collaboration among all the stakeholders who have a role in this important sector.
 9. Although it is not the objective of this discussion paper to provide a detailed analysis of the way forward, the following reflections address some issues in order to facilitate an open discussion particularly in the frame of future developments of the above-mentioned Directive 2002/46/EC:

^{**} The EC Scientific Committee on Food (SCF) has provided a number of opinions in support of existing and planned legislation on certain aspects of food supplements, and this work is being continued in the relevant EFSA Panels (see http://europa.eu.int/comm/food/fs/sc/scf/outcome_en.html).

- As systematic information about the range of botanicals and botanical products present on the market is lacking, consideration could be given, to carrying out a survey to identify the main product categories currently marketed and a study to clarify the potential health-related issues that may need to be addressed.
- In view of the difficulty of compiling a full inventory of botanicals and botanical products, the possibility could also be considered of adopting and regularly updating a list of plants or parts of plants which should not be used or could be put under scrutiny because of the presence of undesirable substances, especially if effective reduction or removal of such substances can not be ensured.
- As purity specifications for all botanicals and botanical preparations are very difficult to define, the development of *ad hoc* manufacturing guidelines, could be considered in order to improve their characterisation and safety. Experience already existing in the pharmaceutical sector could be helpful to this end.
- Considering the importance of providing to consumers adequate information to allow the safe use of botanicals and botanical preparations, the possibility of establishing accredited information sources easily accessible to consumers on these products also deserves attention. A complicating issue in this respect is the diffusion of misleading claims which are very difficult to counterbalance by means of reliable consumer information. However, in this respect, the situation is likely to improve when the proposal for a Community Directive providing for a clear evaluation procedure of “Nutritional and Health Claims” will be adopted.

References

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