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European Legislation on Herbal Medicines

A Look into the Future

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Abstract

Harmonization of the market for herbal medicines is a fundamental requirement for European industries and health professionals and it will also be useful for consumers. Herbal medicines are generally sold as food supplements, but a common regulatory status in the various European countries does not exist. As a consequence, information on clinical indications for use, efficacy and safety are influenced by different opinions, according to the clinical or traditional experience of various folk medicines available in each European country. The European Directive 2004/24/EC released in 2004 by the European Parliament and by the Council of Europe provides the basis for the use of herbal medicines in Europe going forward. The Directive establishes that herbal medicines released in the market need authorization by the national regulatory authorities of each European country and that these products must have a recognized level of safety and efficacy. The safety of herbal medicinal products will be evaluated on the basis of existing scientific literature (data from clinical studies, case reports, pre-clinical studies). When data on safety are not sufficient, it will be communicated to consumers. According to the criteria of safety and efficacy, we will have two kinds of herbal medicinal products in the future: (i) 'well established use herbal medicinal products' (medicinal herbs with a recognized level of safety and efficacy); and (ii) 'traditional use herbal medicinal products'. The later category will include those medicinal herbs that do not have a recognized level of efficacy but are acceptably safe. Even though the fundamental objective of the new European herbal legislation is the harmonization of the market of herbal medicines, important regulations have been introduced, which will contribute to safer use of herbal substances if adopted by the whole of the European community.

Herbal medicines are considered a category of products used for therapeutic purposes that are derived from plants and plant materials. Over the last decade, their increasing global importance has become a topic with both medical and economic implications. The European market for herbal medicines has different rules governing their use in each individual country. They are widely sold and regulated as food supplements. Consequently, the lack of common regulation and their sale as food supplements has meant that the harmonization of their use has been not possible until recently.[1] It can be assumed that this situation has been accepted by the manufacturers and governments but that it is not

convenient for either party. The lack of common regulations in the market creates obstacles for free circulation of products and free concurrence among the manufacturers in Europe.[2,3]

Moreover, information on indications for use, efficacy and safety are often evaluated with different point of views and filtered by different opinions according to the clinical or traditional experience in the various folk medicines in different the European countries.[4] But, in recent times "*a spectre is haunting in Europe...*". This spectre goes by the name of the Directive 2004/EC/24, released in March 2004 by the European Parliament and by the Council of Europe.[5] This directive should be the basis of regulation for the future use of herbal medicines in Europe. Once implemented in the EU Member States, this new Directive should remove the constraints that have made it difficult to grant marketing authorizations of herbal substances and preparations as traditional medicinal products under the pre-existing Community legislation.[6] Briefly, this conference paper summarizes the fundamental topics of the 2004/EC/24.

First of all, the directive establishes that a 'herbal medicinal product' is any medicinal product exclusively containing, as active ingredients, one or more herbal substance, one or more herbal preparation or one or more such herbal substance in combination with one or more such herbal preparation. However, the first real novelty is amending a previous Directive, the 2001/EC/83, by establishing that herbal medicines will need authorization 'like the other medicinals' and, therefore, that they will be released only after the submission of a full application to the national regulatory authorities in European countries.[7]

The results of pre-clinical tests and/or clinical trials conducted with the herbal medicinal product, for which authorization is requested, will not be necessary if the applicant can demonstrate by detailed references to published scientific literature that the constituent (or the constituents) of the product has (or have) a well established medicinal use and that an acceptable level of efficacy and safety is recognized.

It is necessary to pose the question: for how many plants or herbal medicines is it possible to collect evidence showing an acceptable level of safety and efficacy?

A significant number of herbal medicinal products, despite their long tradition of use, do not fulfil the requirements of well established medicinal use. The adverse effects of phytotherapeutic agents are less frequent compared with synthetic drugs; however, well controlled clinical trials and numerous individual case reports have now confirmed that such effects really do exist.[8] The safety of herbal medicines is guaranteed in some cases by long-standing use, but this is not always this case. Modern phytotherapy sometimes includes the intake of new plants or new uses of old plants; therefore, unknown risks can occur.[9]

However, the greatest problem is certainly the evaluation of efficacy of medicinal plants according to the criteria of evidence-based medicine. Their efficacy can be tested in clinical trials much like synthetic drugs, although numerous methodological and logistical problems exist.[10] For a few herbal medicines, efficacy has been established; for many others, this is not the case, mostly because research has not been carried out.[11] The Directive addresses this question by giving manufacturers the opportunity to market herbal medicines for which it is not possible to demonstrate well established use to consumers. These products will be part of a particular category of herbal medicinal products called 'traditional herbal medicinal products', distinguishing them from those having an acceptable level of efficacy, which will be called 'well established use herbal medicinal products'. Taking into consideration the particular characteristics of traditional herbal medicinal products, especially their long tradition, only a special, 'simplified registration' (with respect to that requested for well established use herbal medicinal products) procedure for traditional use will be requested.

Therefore, according to the criteria described by the 2004/EC/24, we shall have a new herbal medicines products classification, including two categories: (i) well established use herbal medicinal prod-

ucts; and (ii) traditional use herbal medicinal products.

When the applicant requires the authorization of a herbal medicinal product, the most important aspects of pre-clinical and clinical aspects (including precautions, warnings and contraindications) of both well established use herbal medicines and traditional herbal medicines used as ingredients of the product will be evaluated. According to the European directive 24/EC/2004, indications for well established medicinal herbs will be the classical clinical indications requiring medical diagnosis. The clinical indications for traditional herbal medicinal products do not recall medical indications. As the 24/EC/2004 recommends,"The therapeutical indications of *traditionals* will be limited to those that can be self-medicated not requiring medical intervention".

Another important aspect regarding traditional products is that the simplified registration should be acceptable only where the herbal medicinal product may rely on a sufficiently long medicinal use in the European Community. At the time of application, these products will have had to have been used for medicinal purposes for a period of 30 years, including 15 years in the European Community. Finally, it is important to remember that the full application of the Directive in Europe is scheduled 7 years after its release in the year 2011; thus, during this transition period, companies may accumulate evidence of medical use for their products.

New aspects contained in the 2004/EC/24, in particular the new classification of herbal medicinal products, will require a change of regulatory competences, both at European and national level. Herbal medicines, previously considered as food supplements and regulated as food, will now be considered as medicinal products. For this reason, the release of the Directive 2004/EC/24 has caused a passage of jurisdiction from European food departments, first to the European Medicines Agency (EMEA) and successively to the national regulatory agencies of drugs of Member States.

A new committee, the Herbal Medicinal Products Committee (HMPC), has been formed inside the EMEA with responsibility for herbal medicinal products. HMPC members are generally but not exclusively nominated by the national regulatory agencies.

Preparing and releasing documents useful to the implementation of the Directive is the fundamental aim of the HMPC work. Documentation produced by HMPC is regularly published in the website of EMEA for public consultation. According to its objectives, the HMPC is preparing a list of herbal substances, preparations and combinations for use in traditional herbal medicinal products. For each herbal substance, the list will contain the indication, the specified strength and the posology, the route of administration and any other information necessary for the safe use of the herbal substance as a traditional medicinal product.

More precisely, these data are contained in the Community monographs for traditional herbal medicinal products, released by the HMPC. A Community herbal monograph is a document that provides a scientific summary of all data available on the safety and efficacy of a herbal substance/preparation intended for medicinal use. In monographs, clinical indications, posology, method of administration, contraindications, precautions use, interactions, data on pregnancy, lactation and children together with other critical aspects are defined for the single medicinal plant.

Community herbal monographs and guidelines for herbal medicines use produced by EMEA are subject to public consultation of all interested parties. These parties are represented by all organizations and individuals, i.e. the pharmaceutical industry, health-care professionals, patients/consumers, their representing organizations or any other interested party, who are interested in the impact of herbal medicine on health. The period of public consultation of EMEA documents provides the opportunity to improve the work on monographs, through criticisms, opinions and suggestions.

In conclusion, the goal of harmonization of the European market of herbal medicines, proposed by the new legislation, introduces important regulations. However, beyond the market aspects, the

adoption of these new regulations by the whole European community is an opportunity that will help contribute to safer use of herbal substances.

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