DIFFERENT LEGISLATION RULES
FOR HERBAL PRODUCTS WITHIN THE EUROPEAN UNION

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It is generally considered that the different countries of the European Union have achieved a harmonization, concerning legislation, that makes all countries seem similar. This harmonization is a fact in certain aspects, but in others the so-claimed harmonization does not exist, and as a result it creates difficulties and comparative offences in the domestic market.

In the specific matter that we are treating, that is Herbal Products, there exists this lack of harmonization which is intended to be solved by means of the Directive 2004/24/EC regarding the Traditional Herbal Medicinal Products.

Let’s make a brief description of the situation concerning Herbal Products legislation in some countries of the European Union before the Directives 2004/27/EU and 2004/24/EU came into force:

UNITED KINGDOM

In the United Kingdom there were four different legal categories of herbs: herbal remedies with a product licence, which could be prescription only, pharmacy only or general sale list medicines; herbal remedies exempt from licensing; herbal products marketed as food supplements; and herbal products marketed as cosmetics. Depending on issues such as claims, presentation and dosage, a single substance could be a food or a medicine. Echinacea, for example, could be marketed as a fully licensed product or as a medicine exempt from licensing; garlic as a food or medicine; and palmetto as a food, a medicine exempt from licensing, or potentially as a fully licensed product.

For industry, there were problems with the current situation in that there were stringent requirements and high costs involved in obtaining a product licence. And, although the other three categories of herbals allowed a way round this, there were problems with each one.

Herbal remedies exempt from licensing were those compounded and supplied by herbalists, which consisted only of dried, comminuted or crushed plants sold under their botanical name with no instructions as to their use. Intended to give herbalists the flexibility to prepare their own herbs for individual patients, exempt preparations could not be produced in quantity or sold under a brand name. In practice, however, this situation was open to misuse, and the UK market was full of these products, although they would not exist forever. Marketing an herb as a food or a cosmetic represented another possibility, but the claims that could be made in both cases were limited.

BELGIUM

The situation in Belgium had been resolved by the passing of the Belgian Herbal Law in 1997. This law regulated herbs under food law and it was strongly challenged by
pharmacists because products sold under food law could be sold in any retail outlet. Pharmacists had a monopoly on medicines and it would have been to their advantage had herbal products come under medicines law.

The law included a list of 365 herbs that could be sold as foods and there was a further list of toxic herbs which could not be sold. Of the 365, 100 were under scrutiny for possible toxic effects. The notification to the ministry of health was necessary before marketing any herbal product. The composition of the product had to be justified, proof had to be provided that it was manufactured according to good manufacturing practice (GMP) standards and the manufacturer had to include a label and any proposed advertising material. In the future, sellers of herbal products would have had to be qualified according to an accredited programme.

**GERMANY**

In Germany, almost all herbals were medicines, although many were registered according to a "simplified registration procedure". This procedure had arisen as a result of the German medicines law of 1978 in which all medicines on the market at that time had to be assessed and re-registered.

However, the system for doing this was so slow - and for herbs the required efficacy data did not always exist - that in 1994 the scope of the law was widened, such that preparations with a long history of use could be registered according to a simplified procedure. These "traditional use" products included many herbs, and about 1,700 of these had now been registered.

The other routes to registration of herbals in Germany were as prescription medicines, in which case robust clinical trial data were needed, or as over-the-counter medicines using what was known as a standard authorisation procedure, which cited official monographs as "evidence". However, only products on the market before 1978 and containing prophylactic or mildly effective herbs were regarded as "traditional use" products. These could also be registered as medicines. Few herbals were foods. Foods had to be presented as foods - not pharmaceutical products - and could not make medical claims.

**SPAIN**

An important issue to the industry in Spain was the channel of distribution for herbals. There were two categories of herbs in Spain: medicinal herbs, which legally could be sold only in pharmacies, and phytotraditional products, which could be sold in other outlets.

However, there was a problem in distinguishing between medicinal herbs and traditional products. There were also products containing mixtures of herbs with other ingredients, which did not fall into either category. Moreover, in practice, herbalists and health food shops actually sold all kinds of herbs - both medicinal and traditional. What the industry wanted was the freedom to sell herbals outside of pharmacies and to be able to make claims for their use. The industry did not want herbals to be categorised as medicines because that meant that they would be restricted to
pharmacy only sale. And it was hoped that they would be classified either as foods or as a special category.

**SWEDEN**

Special legislation for herbal products had existed in Sweden since 1978, and in 1993 they were classified by the regulatory authorities as medicines.

Earlier legislation had not allowed claims for herbals, but current regulations allowed for 64 claims to be applied to particular products. Thus, both garlic and *Echinacea* could make a claim for "traditional use for soothing symptoms of coughs and colds" and *Ginkgo biloba* for the "treatment of prolonged symptoms in elderly persons such as failing memory, dizziness and tinnitus."

More than 100 herbal remedies had now been registered as medicines by the Swedish medical agency, and all these products could make claims. However, huge "grey areas" still existed, including the 200 or so natural products that had been regulated according to older legislation, and a number of products marketed as foods, for which no claims could be made.

**ITALY**

In Italy, a proposal for a new legal category for herbals was currently being considered by the government. If this law was passed, herbals would be neither foods nor medicines.

There was a long tradition of herbal use in Italy and herbs were available in both pharmacies and non-pharmacy outlets. Those herbs with pharmacological activity were licensed as medicines and available in pharmacies only, while non-medicinal herbs, for which there was a large market, were channelled through outlets known as herbalists. The new proposals also stated that all retailers of the "new category" must either be pharmacists or have a diploma (which involved three years of study at university) in herbal techniques. Pharmacists would not have exclusive rights to selling these "new category" products and the law, if passed, would enable the continued supply of herbal products through herbalists, although they would have to be qualified.

**THE NETHERLANDS**

The situation in Holland as simple in that herbals could be either foods or medicines. Most were foods, which were sold mainly through drug stores, with only a small amount being sold in pharmacies.

However, the situation was more complex than it seemed in that there were new regulations for foods, which covered issues of safety and claims. In terms of safety, there was now a negative list of herbs which were considered to be too toxic to be sold as foods. A list of allowable health claims had also been developed. Although "splitting hairs," the statement "promotes blood flow" was considered to be a health claim, while "promotes the production of white blood cells" was a medicinal claim. "Breathe more freely" was judged to be a health claim, while "breathe freely" was a medicinal claim.
"Used for inner anxiety" was a health claim and "for difficulty in concentrating" a medicinal claim.

The current situation did not please everyone and preparatory work had been done on the possibility of registering herbs as medicines. The attitude of the Dutch regulatory authorities was to wait for European legislation, but there was need in the meantime to protect public health. "The world is changing. Foods are increasingly taken for health as well as nutritional purposes and the separation between foods and medicines is eroding."

As it can be seen, the situation is different depending on the country. Roughly speaking we may distinguish between two main groups of countries: on one side there are the Anglo-Saxon countries (United Kingdom, Germany, Holland and so on) with a more permissive legislation, and on the other side, those countries of Latin tradition (Italy, Spain, France, and so on) that are much more restrictive in the subject we are treating.

The aim of the Community Directive 2004/24/UE is to harmonize this situation so we are going to comment it succinctly:

The 30th of April 2004, the European Commission published the Directive 2004/24/EC on traditional herbal medicinal products (the Herbal Directive), which amends the existing legislation on medicinal products, Directive 2001/83/EC, as amended by Directive 2004/27/EC. Member states had to implement the Herbal Directive by the 30th of October 2005. The Traditional Use Registration will only apply to an herbal medicinal product that:

(a) has an indication “exclusively appropriate” to a traditional herbal medicinal product and is intended and designed to be used without supervision of a medical practitioner;
(b) is exclusively for administration in accordance with a specified strength and posology;
(c) is an oral, external or inhalation preparation;
(d) satisfies the period of “traditional use”;
(e) has adequate data to support the traditional use (i.e. it must not be harmful if used as indicated, and its pharmacological effects or efficacy must be plausible based on long-standing use).

The Traditional Use Registration will not apply where national regulatory authorities judge that a herbal medicinal product satisfies the requirements for obtaining a marketing authorisation under the amended Directive 2001/83/EC, for instance under the bibliographical authorisation procedure. The latter is available when the active ingredient has a "well-established medicinal use" within the EU for at least ten years, with recognised efficacy and an acceptable level of safety under Annex I of amended Directive 2001/83/EC. Companies will need guidance from the Committee on Herbal Medicinal Products (HMPC) on the scope of the two review procedures and, in practice, there may be some overlap.
The Traditional Use Registration will also not apply to homeopathic products that fulfil the criteria for standard medicinal product marketing authorisations or for homeopathic registrations under amended Directive 2001/83/EC.

The Herbal Directive allows the registration of traditional herbal medicinal products that also contain vitamins and minerals, providing that their action is ancillary to the active ingredient and only where proven safe. This potentially covers several products currently sold as dietary supplements. Other active ingredients cannot be used.

The Herbal Directive relates to herbal products that are medicinal. Which products will be considered medicinal is unclear, because some products can be sold in other categories depending on their presentation. Categorisation criteria include: effects of the ingredients, the manner in which the product is presented and promoted, whether claims are made to treat or prevent disease, the product form, directions for use, and possible risks to consumers. Because the criteria are vague, they lead to different results in different member states. The Commission is organising a workshop to reach a more unified approach, but establishing a single practice will take time. For now, companies must rely on precedents and statements by national regulators.

The recitals to the Herbal Directive state that those non-medicinal herbal products which fulfil EU food legislation criteria will continue to be regulated under that legislation. Culinary herbs and certain other plants can therefore continue to be sold as food supplements. Examples include garlic, ginseng and *Garcinia cambogia*. However, companies wishing to make medicinal claims may be able to register such products under the Herbal Directive.

Traditional herbal medicines will need to meet specific standards of safety and quality, and to demonstrate their traditional use. These standards are lower than those that apply to innovative medicines, and are intended to be more flexible than those governing bibliographical applications. The Herbal Directive does not specify a dossier form but member state authorities will probably follow the Common Technical Document format used for other medicinal products.

The HMPC and the Commission will establish a positive list of herbal substances, preparations and combinations to be used in traditional herbal medicines (the List). The List will contain for each substance: the therapeutic indication; specified strength and posology; route of administration; and other relevant safety information. For those products containing a substance on the List, applicants may refer to the List without having to demonstrate traditional use or safety, but administrative and quality data will still need to be submitted. It is unclear how the List will be used for combinations.

To promote harmonisation, member states will be required to recognise registrations of herbal medicinal products granted by other member states consisting of substances contained on the List (or covered by an HMPC monograph).

For products not covered in all aspects by the List, the applicant will have to submit data supporting traditional use and safety. Traditional use must be supported by bibliographic or expert evidence that the product, or corresponding product, has been in medicinal use for at least 30 years. At least 15 of the 30 years must have been in the EU.
The Herbal Directive defines “corresponding product” as one having the same active ingredients, the same or similar purpose, equivalent strength and posology, and the same or similar route of administration. The 30-year requirement is satisfied even if the product was marketed without specific authorisation or if the number or quantity of ingredients of the product has been reduced over the 30-year period. If the product (or corresponding product) meets all but the 15-years-in-the-EU requirement, it may be referred to the HMPC, which may reduce that requirement. If possible, the HMPC will establish an EU-wide herbal monograph. Evidence can derive from many sources, such as herbal experts, current textbooks, pharmacopoeias, published information referring to specific product formulations (for example, the Martindale List of Preparations), and company archive material (i.e. brochures and invoices).

To demonstrate safety, a bibliographic review of relevant data and an expert report will be required. Regulatory authorities may request additional data when, for example, there are specific concerns regarding safety, an ingredient is relatively unfamiliar to science, or the medicine has been used predominantly in countries where there is no reporting system, a shorter life expectancy or a significantly different gene pool.

It is difficult to predict the length of a typical Traditional Use Registration procedure. One would expect it to take between 6 and 12 months – the time it takes for a “well-established use” bibliographical application. Obviously, the process will be quicker for applications using the List.

The HMPC met for the first time in September 2004 and includes experts in herbal medicinal products. It has broad control over the Traditional Use Registration procedure, and is also responsible for authorising herbal medicinal products under the general bibliographical application rules of amended Directive 2001/83/EC.

The HMPC assumed this role from the Committee for Medicinal Products for Human Use (CHMP) Working Party on Herbal Medicinal Products. In order to ensure appropriate communication between the CHMP and the HMPC, the executive director of the agency will set up a formal co-ordination procedure.

The labelling and leaflet information and advertising of products with a Traditional Use Registration will need to meet the requirements in amended Directive 2001/83/EC. Furthermore, the Herbal Directive requires labelling and leaflets to state clearly that the indications are based on information obtained from long-standing use – not scientific data – and users must be advised to consult a qualified practitioner if symptoms persist. The Herbal Directive also requires any advertisement to indicate: … traditional herbal medicinal product for use in specified indication(s) exclusively based upon long-standing use.

The quality requirements applicable to licensed medicines will apply to Traditional Use Registration products. In particular, manufacturers will need to comply with the principles of Good Manufacturing Practice (GMP) and to hold a manufacturer’s licence or a wholesale dealer’s licence, where appropriate. Manufacturers and importers must employ at least one qualified person who is able to certify that GMP standards have been met.

Member states had to introduce a Traditional Use Registration scheme by 30 October 2005. Once they have implemented the new rules, industrially produced herbal...
medicines (including over-the-counter remedies sold in supermarkets, health food stores, etc) will require either standard medicinal product marketing authorisation or a Traditional Use Registration. Herbal medicinal products that were on the EU market on 30 April 2004 will benefit from a seven-year transition period before they must comply with the new rules, subject to stricter national rules. During the transition period, companies may accumulate evidence of traditional use. Time is also allowed for stock depletion.

Hence an unlicensed product marketed prior to implementation of the Herbal Directive may be sold after implementation. Until national implementation (or until the expiration of transitional protection), products must continue to comply with national law.

The new rules are the result of over five years of discussion at both European and member state level. Their goal is to provide greater health protection, increase consumer confidence in traditional herbal medicinal products and encourage a single market for these products. Although beneficial for consumers, the new rules are likely to hinder small manufacturers. Not only will companies have to manufacture and market their herbal products to recognised standards, they will also incur costs of inspections, upgrades to machinery and premises, and licensing and registration fees. Companies should consider whether their products fall under the scope of the new rules and, if so, the information they will need to submit. Also, companies wishing to reposition a product as medicine in order to make minor medicinal claims should identify reasonable evidence that their product (or corresponding product) has traditionally had medicinal use. Discussions are continuing about legal categorisation and the types of product claims available. Of particular interest are the herbal monographs that the HMPC is currently producing. For products not eligible for the Traditional Use Registration, it will be possible to submit an abridged application for a standard product marketing authorisation based on “well-established medicinal use’ and refer, at least in part, to an herbal monograph.

As we have observed, the community directive is in force but reality is quite different. Therefore we see that actually the Spanish Health Authorities, for example, consider that Traditional Chinese Medicine products due to its ingredients features (medicinal plants not included in the Ministerial Order of 1973), have the rank of medicines and consequently require a previous evaluation by the Spanish Drugs Agency, completely forgetting that those products are free trade products in other member states of the European Union.

The Directive 2004/24/EC of the European Parliament and of the Council of 31 March 2004 amending, as regards traditional medicines made of plants, Directive 2001/83/EC on the Community code relating to medicines for human use, in its section 2.1 states that the Member States have to adopt the necessary dispositions in order to enforce all terms set up in the mentioned Directive before the 30th of October of 2005.

Moreover, section 2.2 of the abovementioned Directive establishes that in the case of those traditional medicines made of plants, referred to in article 1, which would already be in the market when this Directive entered into force, the competent authorities would have to apply all terms provided in the mentioned Directive in a period of 7 years from the day that it enters into force. For all that, we understand that since the Spanish state did not set up any legislation before the 30th of October of 2005 as it is provided by
Directive 2004/24/EC of the European Parliament and of the Council of 31 March 2004, it impedes the commercialization with those TCM products that were already in the market.

As we have just observed, the Spanish Drugs Agency considers Chinese Herbal Products as medicines. There are also certain Chinese plants that cannot be sold as they are included in the Order SCO/190/2004 that states a list of plants which trade is totally forbidden because of their toxicity.

Chinese Herbal Products cannot be sold in Spain as food supplements, as the Royal Spanish Decree 1275/2003 does not permit galenic preparations made of vegetal species. It is not either permitted to sale them as food or dietetic products.

They cannot be sold as traditional Chinese Herbs in that Ministerial Order of 3 of October of 1973 states a positive list of preparations made of medicinal vegetal species, where TCM formula are not included.

The situation in other countries as France, Italy, Greece, Portugal and Eastern European countries, is quite similar to the Spanish. We aren't afraid to affirm with confidence that in these countries the attitude of the authorities will be less favourable to permit the registration of Chinese Herbal Products according to the dispositions of the Directive 2004/24/EC. On the other hand, in these countries the regulation of Food Supplements is also very restrictive for TCM products as a result of the fact that most of the Chinese Herbs are not included in the positive lists that each country has established.

In conclusion, for the European Comission the original aim of the Directive was to create an easier path to the herbal industry but it is being turned around by the Committee for Herbal Medicinal Products and some member states. On its hand, Committee for Herbal Medicinal Products is slow to produce the monographs and as other member states like Germany, it requests extra testing (for example, the genotoxicity). On the other hand, not all member states have already implemented the Directive 2004/24/EC, in particular 6 of the European member states have not implemented it yet.

The European Commission invited stakeholders to exchange views and the ECCTCM was one of the organizations invited. Our opinion is reflected in the Commission’s Report for the European Parliament. In page number 5 of the Commission’s Report there appears the number of applications and registrations, but I can bring you forward that it is very low. If you want a copy of the European Commission’s Report and the Conference Report, do not hesitate to ask me for it in the e-mail that will be shown in the last slide.

Taking into account everything before mentioned, another Community Directive becomes interesting, the 2004/27/EC. The Co-ordination Group for Mutual Recognition and Decentralised Procedures – Human, CMD(h), has been set up in the revised Pharmaceutical Legislation (Directive 2004/27/EC amending Directive 2001/83/EC) for the examination of any question relating to marketing authorisation of a medicinal product in two or more Member States in accordance with the mutual recognition procedure or the decentralised procedure.
The CMD(h) has also the following specific responsibilities, as laid down in the revised Pharmaceutical Legislation:

- In case of disagreement between the Member States involved in a Mutual recognition or decentralised procedure on the Assessment report, the summary of product characteristics, the labelling or the package leaflet on the grounds of “potential serious risk to public health”, the points of disagreement are considered by the CMD(h). The CMD(h) uses its best endeavours to reach agreement on the action to be taken within the 60 day time period foreseen in the legislation.
- To lay down, yearly, a list of medicinal products for which a harmonised summary of product characteristics should be drawn up, to promote harmonisation of marketing authorisations across the Community.

The CMD(h) started its activities in November 2005 and replaced the informal Mutual Recognition Facilitation Group, which was in operation over 10 years, to coordinate and facilitate the operation of the mutual recognition procedure.

The CMD(h) is composed of one representative per Member State, including Norway, Iceland and Liechtenstein, appointed for a renewal period of three years. The list of the CMD(h) Members, together with the respective professional qualifications is published on the CMD(h) website. Observers from the European Commission and accession countries also participate in the meetings of the CMD(h).

The CMD(h) holds monthly meetings at the European Medicines Agency. The CMD(h) meetings take place on the week of the CHMP and have a duration of 2 to 3 days, which reflects the extended scope of CMD(h) activities compared to the informal Mutual Recognition Facilitation Group. The European Medicines Agency is responsible for providing the secretariat of the CMD(h).

Approximately half of the time of the CMD(h) meeting is dedicated to discussions on procedural/regulatory issues, development of Guidance documents and oversight of the activities of the various CMD(h) Sub-groups/Working groups whilst the other half is devoted to trying to reach agreement for applications referred to the CMD(h), in case of disagreement between Member States on the grounds of a potential serious risk to public health.

Prior to the entry into force of the revised Pharmaceutical Legislation, the Heads of Agencies set up an ad hoc Working Group, to consider the role of the new Co-ordination Groups for Mutual recognition and decentralised procedures. The report from this ad hoc Working Group is available on the Heads of Medicines Agencies website.
The Heads of Agencies agreed that the mission of the CMD(h) would be:

- To aim for consensus and avoid referrals to the CHMP other than in exceptional cases of disagreement on the grounds of “potential serious risk to public health”;
- To ensure consistency of standards and good quality decision making across the EU in the interests of public health;
- To achieve the harmonisation of SPCs of nationally authorised products in particular cases that would benefit citizens of the Community;
- To present a harmonised view on the interpretation of Directives and Regulations in order to facilitate implementation and finding solutions.

Press releases with statistics, guidance documents, Q&As and information on applications referred to the CMD(h) are published monthly on the CMD(h) website.

The CMD(h) also publishes, on a yearly basis, a summary of the activities carried out by the CMD(h) and yearly statistics for new applications in the Mutual recognition and Decentralised procedures and for the applications referred to the CMD(h).

The existence of the Co-ordination Group for Mutual Recognition and Decentralised Procedures – Human, CMD(h) is of relevant importance, due to the statement in the 4th chapter in the Directive 2004/24/EU of the Mutual recognition procedure and decentralised procedure.

The Decentralised and Mutual recognition procedures are European authorisation procedures based on the principle of recognition of the assessment by the Reference Member State (RMS).

**Mutual Recognition Procedure**

In the case of the Mutual Recognition Procedure, the RMS has already issued a marketing authorisation. The RMS’s assessment report forms the basis for requesting the other Member States' mutual recognition of the marketing authorisation (including the Summary of Product Characteristics (SPC), package leaflet and labelling text), unless they have objections on the grounds of a potentially serious risk to public health. In such situations, further discussions will be held in the Coordination group for Mutual recognition and Decentralised procedures (CMD(h)).

**Decentralised procedure**

The Decentralised Procedure may be used to obtain a marketing authorisation in several Member States when the applicant does not yet have a marketing authorisation in any country. The applicant requests one country to be the Reference Member State (RMS) in the procedure. On the 120th day of the assessment procedure, the RMS circulates the Draft assessment report, including comments on the SPC, package leaflet and labelling texts. There is also a Mutual Recognition Procedure during the next 90 days, in which other Member States generally adopt the RMS's assessment, unless they have important objections on the grounds of a potentially serious risk to public health. In such situations, further discussions will also be held in the Coordination group for Mutual recognition and Decentralised procedures (CMD(h)).
As to conclude and on the basis of all mentioned and of my personal experience and knowledge in this matter, for those of you who wish to access to the European Union market I will say, as a recommendation, from the legal perspective, choose a country in the EU where to register its products, and afterwards use the Mutual Recognition Procedure for its registration in the other countries. The chosen country has to be in the Anglo-Saxon area and, in my opinion, the most convenient is Holland.