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Homeopathic Medicinal Products

**Commission Report to the European Parliament and Council on the
Application of Directives 92/73 and 92/74**

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1. Background:

Over the past 30-40 years homeopathy has benefited from growing demand both from doctors and from the public in the majority of European countries. Three Europeans out of four know about homeopathy and of these 29% use it for their health care. Homeopathic medicinal products today account for a little over 1% of the gross sales of the European pharmaceutical industry. In France, Germany and The Netherlands this figure is over 2% in value and 5% by volume.

In 1992 the Council adopted Directives 92/73¹ and 92/74² on homeopathic medicinal products. There were several reasons for creating specific provisions for homeopathic medicinal products: Homeopathic medicine was officially recognized in certain Member States but was only tolerated in other Member States. Even if homeopathic medicinal products were not always officially recognized, they were nevertheless prescribed and used in all Member States. Considerable differences in the status of alternative medicines hindered trade in homeopathic medicinal products within the Community and lead to discrimination and distortion of competition between manufacturers of these products. Moreover, taking account of the particular characteristics of homeopathic medicinal products, such as the very low level of active principles they contain and the difficulty of applying to them the conventional statistical methods relating to clinical trials, the regulatory framework for medicinal products (in particular the provisions of Directive 65/65/EEC³ and Directive 75/319/EEC⁴) seemed to be not always appropriate for homeopathic medicinal products.

¹ Council Directive 92/73/EEC of 22 September 1992 widening the scope of Directives 65/65/EEC and 75/319/EEC on the approximation of provisions laid down by law, regulation or administrative action relating to medicinal products and laying down additional provisions on homeopathic medicinal products, OJ. L297, 13/10/1992 p. 8

² Council Directive 92/74/EEC of 22 September 1992 widening the scope of Directive 81/851/EEC on the approximation of provisions laid down by law, regulation or administrative action relating to veterinary medicinal products and laying down additional provisions on homeopathic veterinary medicinal products, OJ. L297, 13/10/1992 p. 12

³ Council Directive 65/65/EEC of 26 January 1965 on the approximation of provisions laid down by law, regulation or administrative action relating to proprietary medicinal products, OJ.22, 09/02/1965 p. 369

⁴ Council Directive 75/319/EEC of 20 May 1975 on the approximation of provisions laid down by law, regulation or administrative action relating medicinal products, OJ. L147, 09/06/1975 p. 13

By means of Directives 92/73 and 92/74 it was intended to create a legal frame that would allow patients access to the medicinal products of their choice provided all precautions are taken to ensure the quality and safety of the said products; to provide users of these medicinal products with a very clear indication of their homeopathic character and with sufficient guarantees of their quality and safety and to harmonize the rules relating to the manufacture, control and inspection of homeopathic medicinal products to permit the circulation throughout the Community of medicinal products which are safe and of good quality.

To this end, Directives 92/73 and 92/74 provided for the creation of a special, simplified registration procedure in Member States for those traditional homeopathic medicinal products which are placed on the market without therapeutic indications in a pharmaceutical form and dosage which do not present a risk for the patient. Regarding homeopathic medicinal products with therapeutic indications or in a form which may present risks, the usual rules governing the authorization to market medicinal products should be applied. Member States which had a homeopathic tradition should be, however, able to apply particular rules for the evaluation of the results of tests and trials intended to establish the safety and efficacy of these medicinal products.

According to Article 10 paragraph 3 of Directives 92/73 and 92/74, the Commission should, not later than 31 December 1995, present a report to the European Parliament and the Council concerning the application of the Directives. Given that on 31st December 1995, the date by which this report should have been presented, not all Member States had notified the Commission of the full application of the Directives, the Commission decided to put back the completion of the study until the end of 1996 in order to be able to take onboard the practical experiences in some Member States that were late in transposing the Directives. As this report is drafted, (January 1997) most Member States have notified implementation of both Directives. Infringement procedures concerning full or partial non-transposition had to be started (and are still under way) against Belgium and France regarding Directive 92/73 and against Belgium, France, Portugal and the United Kingdom regarding Directive 92/74.

The analysis which follows is based on an in-depth study on the application of Directives 92/73 and 92/74 performed by independent consultants on behalf of the European Commission. It will show a certain degree of disparity in the application of the Directives in Member States and contradictions in the interpretation thereof. Therefore, in its conclusion, this report will ask the European Council and Parliament to express their view on particular problems and to consider whether certain amendments would help to fully achieve the initial objectives.

2. Application of Directive 92/73 (homeopathics for human use):

Definition of homeopathic medicinal product:

According to Article 1 of Directive 92/73 '*homeopathic medicinal product*' shall mean any medicinal product prepared from products, substances or compositions called homeopathic stocks in accordance with a homeopathic manufacturing procedure described by the European Pharmacopoeia or, in absence thereof, by the pharmacopoeias currently used officially in the Member States. Homeopathic medicinal products may also contain a number of principles.

All countries have accepted this definition of homeopathic medicinal product when transposing this Article. Ireland alone has not transposed paragraph 2 of Article 1 "A homeopathic medicinal product may also contain a number of principles". The status of a homeopathic medicinal product is henceforth recognised throughout the European Union, since Member States have adopted and accepted an identical definition. Therefore no need for further Community action with regard to this definition arises.

Manufacture, control and inspection, information exchange:

Only some Member States have transposed the relevant Articles 3 - 5 of Directive 92/73 with complete clarity. The absence of transposition in other Member States can be explained on the basis of the application and transposition of Directive 75/319/EEC, prior to Directive 92/73/EEC, in particular chapters IV referring to manufacture and imports coming from third countries and chapter V referring to supervision and sanctions. Taking into account that no complaints or new suggestions with regard to these Articles have been received by the Commission, it seems to be acceptable to leave these Articles as they are.

Placing on the market of homeopathic medicinal products - Registration and Authorization:

Article 6 paragraph 1 of Directive 92/73 obliges Member States to ensure that homeopathic medicinal products manufactured and placed on the market within the Community are registered or authorized in accordance with the provisions of Directive 92/73. Moreover it is foreseen that "Each Member State shall take due account of registrations and authorizations previously granted by another Member State."

All countries have transposed this paragraph. Henceforth homeopathic medicinal products put on the market in the European Union must have either a registration or an authorization. However, the interpretation of the formulation « Each Member State shall take due account of registrations and authorizations previously granted by another Member State » varies among Member States:

- Denmark interprets it very widely on the basis of mutual recognition, accepting without any restriction homeopathic medicinal products that have already obtained registration or authorization in another Member State.
- Germany follows the Danish line, but does not accept mutual recognition unless the product meets all national criteria, for example being included in traditional German homeopathy. Consequently, there is no real mutual recognition.
- Sweden takes account of registrations and authorizations already granted and allows the submission of a simplified dossier, provided the applicant shows that the product submitted for registration has been present on the market for at least ten years in another Member State.
- For other countries, registrations and authorizations delivered by other Member States are only taken into account when a registration is submitted and this is purely an administrative acknowledgement, with neither mutual recognition nor simplification of administrative procedures.

According to manufacturers' opinions supported by consumers and doctors organisations, the wording « shall take due account of registrations... » does not guarantee mutual recognition of registrations of homeopathic medicinal products by other Member States. The wording « take account of » is not precise enough to impose a clear and unambiguous obligation on Member States. As a result it would

induce a barrier to the Single Market of homeopathic medicinal products and there would be need for legislative activities on Community level.

Abstention from the introduction of a simplified registration procedure):

No Member State informed the Commission to make use of the possibility (provided for in Article 6 paragraph 2), to abstain from the introduction of a simplified registration procedure. Therefore this provision is presently not applicable.

Placing on the market - Advertising:

Article 6 paragraph 3 leaves Member States the choice of allowing advertising for homeopathic medicinal products subject to the provisions of Directive 92/28⁵ on the advertising of medicinal products and some special conditions stated in Article 6 paragraph 3, or forbidding all advertising for the above mentioned medicinal products. Three countries (Austria, Italy and Luxemburg) have chosen to forbid all advertising. Five countries (France, Germany, the Netherlands, Spain and the United Kingdom) allow advertising in line with Article 6 paragraph 3. Denmark authorizes advertising for the medical profession but forbids it for consumers and Belgium, Ireland, Portugal and Sweden have not explicitly transposed this article. Since this article is optional, it is not surprising to find that provisions differ from Member State to Member State. Taking into account that no complaints or new suggestions with regard to this paragraph have been received by the Commission, it is acceptable to leave the paragraph as it is.

Eligibility for the simplified registration procedure:

According to Article 7 paragraph 1 "*only homeopathic medicinal products which satisfy all of the following conditions may be subject to a special, simplified registration procedure:*

- they are administered orally or externally,
- no specific therapeutic indication appears on the labelling of the medicinal product or in any information relating thereto,
- there is a sufficient degree of dilution to guarantee the safety of the medicinal product; in particular, the medicinal product may not contain either more than one part per 10.000 (D4) of the mother tincture or more than 1/100th of the smallest dose used in allopathy with regard to active principles whose presence in an allopathic medicinal product results in the obligation to submit a doctor's prescription."

All Member States have paid attention to this article, but some of them have laid out own dispositions concerning routes of administration and registerable dilutions: Some countries (Denmark, Finland, Luxemburg, the Netherlands, Portugal, Spain and Sweden) have transposed the article as it stands but others have introduced modifications or precisions:

Modifications concerning the routes of administration:

In France, homeopathic medicinal products administered by subcutaneous injection can be registered according to specific rules. In Italy and the United Kingdom injections are explicitly excluded. Italy goes further, also excluding transdermal

⁵ Directive 92/28/EEC of 31 March 1992 on the advertising of medicinal products for human use, OJ L113, 31/03/1992, p.13

administration (patches). Although accepted for the simplified registration procedure in some other Member States, in Finland eye drops and suppositories must be authorised according to the standard procedure.

Modifications concerning registerable dilutions:

In Austria, only substances described in a pharmacopoeia of the EEA may be registered and a list of substances has been established specifying the minimum registerable dilutions. These dilutions go from D1 (1/10) to D8 (1/100.000.000). In Germany, the registerable dilution thresholds have been replaced by the requirement of "an absence of harmful effects". What is more, the registration of a homeopathic medicinal product can be refused if it does not meet all of the criteria defined by the German authorities (ie: being generally known for homeopathic or antroposophic use). The United Kingdom and Ireland have fixed the dilution threshold to D4 (1/10.000) for all products submitted to a simplified registration.

Even though the European Commission gave an interpretative clarification concerning the registerable dilutions⁶, it is noticeable that there is a large degree of difference of interpretation between transpositions at national level. This results in different systems of registration, some of which are more open than the others and allow the registration of a greater range of homeopathic medicinal products.

Manufacturers, doctors and consumers' agree, that if it was not possible to register mother tinctures and dilutions between D1 (1/10) and D4 (1/10.000) a high percentage of single and complex homeopathic medicinal products would have to be withdrawn or have to be changed, as one or more active ingredients are in a potency lower than D4 (1/10.000). The companies would have to create new formulas and start the research and development period from the beginning concerning the clinical data and the empirical knowledge of these homeopathic medicinal products. Therefore, a clarification that the threshold of D4 applied only to active principles whose presence in an allopathic medicinal product results in the obligation to submit a doctor's prescription or a more flexible solution (like the Austrian approach with lists of registerable substances) is asked for. Moreover it has to be stated that lack of harmonised Community lists of active principles whose presence in an allopathic medicinal product results in the obligation to submit a doctor's prescription leads to disharmony in the application of the present provision.

Likewise it was criticized that the Directive limits the simplified registration procedure to homeopathic medicinal products whose route of administration is oral or external. According to some opinions it should be applicable to other pharmaceutical forms. Thus such routes of administration as subcutaneous administration, or nasal spray, should be registerable under a simplified procedure. In this context it has been stressed that the homeopathic industry states that it could refer to a safe and secure experience with a simplified registration for the parenteral pharmaceutical form. Those who propose an extension of the simplified registration procedure to other routes of administration stress in particular the fact that Chapters IV and V of Directive 75/319 and the principles and guidelines of good manufacturing practice are fully applicable to all homeopathic medicinal products.

⁶ see: answer of the Commission to written question E-2804/95, OJ C66, 4.3.1996, p.31

Labelling and package insert:

Article 7 paragraph 2 of Directive 92/73 states that in addition to the clear mention of the words 'homeopathic medicinal product', the labelling and, where appropriate, package insert for homeopathics subject to a simplified registration shall bear certain specified, and no other, information (including the phrase "*homeopathic medicinal product without approved therapeutic indication*").

Most Member States have transposed this Article without modification. Some have, however, slightly divergent provisions in their national transposition. So, in Denmark, the clause "*homeopathic medicinal product without approved therapeutic indication*" is replaced by "Homeopathic medicinal product, whose efficacy is not documented", in Finland, this clause is not mentioned in the regulations for labelling, in Germany, the term "approved" does not appear and in the Netherlands, the applicant has the choice between the terms "approved" and "specific". In addition, the requirement of including the registration number is absent from the labelling regulations in Denmark.

Manufacturers, doctors and consumers criticize that the Directive excludes fantasy names for preparations combining a number of substances. Inclusion of all the scientific names on the label of a preparation would make an identification difficult if not impossible. It was also pointed out that the Directive specified the inclusion of the method of administration on the labelling and package insert and that this should also include the dosage where appropriate. The clause "without therapeutic indication" was criticized for being misleading and was generally seen as the most controversial issue in the context of labelling of homeopathics.

Content of the application dossier for a simplified registration

Article 8 of Directive 92/73 outlines the documents that have to be included with the application for a simplified registration. Most countries have correctly transposed this Article. However, two Member States, France and Ireland, have stricter interpretations of the Directive: In France, the documents to be supplied are more numerous and the registration dossier is closer to a standard application for a marketing authorization. The "usual denomination" can be used for registration purposes. Homeopathic medicinal products other than those intended for oral or external use, in particular subcutaneous injectables, can be registered through a separate application that justifies the necessity of using the routes of administration concerned. In Ireland, supplementary requirements concerning the person responsible for placing the product on the market and the manufacturer, whose identity must be clearly discernible, have been established.

Apart from current French legislation according to which the simplified registration dossier is close to a standard application dossier for authorization, the transposition of this Article poses no particular problems.

Marketing authorization and specific rules for homeopathic medicinal products:

According to Article 9 of Directive 92/73, homeopathic medicinal products not subject to the simplified registration procedure shall be authorized and labelled in accordance with Directive 65/65 including the provisions concerning proof of therapeutic effect. However, Article 9 paragraph 2 gives Member States the possibility to introduce or retain in their territory specific rules for the pharmacological and toxicological tests and clinical trials in accordance with the

principles and characteristics of homeopathy as practised in that Member State. Austria, France and the Netherlands accordingly provide for specific rules which take account of the character of homeopathic medicinal products and their traditional forms of use; Germany has established monographs and elaborated guidelines for clinical tests which are equally valid for homeopathic medicinal products subject to registration; Italy has created a commission charged with defining specific norms for the authorization and labelling of homeopathic medicinal products other than those covered by Article 7 paragraph 1 of the Directive; Spain mentions in its transposition that "account will be taken of the homeopathic nature of medicinal products during the evaluation of the tests". Other Member States have not specifically transposed this Article.

It seems that some countries have not transposed this Article because general regulations already included homeopathic medicinal products subject to authorization. As the introduction of specific rules is not obligatory, most Member States have not taken clear action. Only Germany has clearly defined these rules, because of its own homeopathic tradition. France and Spain remain vague and Italy and the Netherlands have still not named a commission charged with developing these rules.

Manufacturers are concerned that Article 9 is optional and not binding on Member States and that the formulation in Article 9 paragraph 2 "*specific rules in accordance with the characteristics of homeopathy...*" is too vague. Therefore a Single Market for homeopathic medicinal products with therapeutic indications would be impossible. They have asked that it should be clearly stated that these specific rules should provide for the involvement of appropriate experts in homeopathic and anthroposophic medicine and that Article 9 paragraph 2 should become a binding provision.

3. Application of Directive 92/74 (homeopathics for veterinary use):

The structure and wording of Directive 92/74 on homeopathic veterinary medicinal products is nearly identical to the text of Directive 92/73 on homeopathics for human use. Therefore it is no surprise that the problems and results outlined above with regard to homeopathics for human use can be - *mutatis mutandis* - fully applied to the application of Directive 92/74 on homeopathic veterinary medicinal products.

There is, however, one specific requirement concerning the eligibility for the simplified registration procedure of homeopathic medicinal products for veterinary use that has given rise to criticism from interested parties: Article 7 paragraph 1 of Directive 92/74 requires that the products eligible for the simplified registration "*are intended for administration to pet animals or exotic species whose flesh or products are not intended for human consumption*" and thereby excludes the simplified registration procedure for homeopathics intended to be administered to food producing animals.

4. Conclusions:

It has been shown that starting from regulatory texts whose objectives were very clearly expressed in 1992 - to achieve the harmonisation of regulations for homeopathic medicinal products and enable their free circulation - a certain but not yet satisfying degree of harmonisation has been achieved in 1997.

Following practical experience with the implementation of Directives 92/73 and 92/74, the enlargement of the EU and changes in opinions within Member States, Council and Parliament may have different views on certain points today from the positions taken in 1992. Before presenting any concrete proposal for an amendment to Directives 92/73 and 92/74 and in order to determine feasible solutions to the problems raised in this report, the European Commission invites the European Parliament and Council to express their views and positions on the following suggestions in their response to this report:

- The wording of Article 6 paragraph 1 (of Directives 92/73 and 92/74) "*Each Member State shall take due account of registrations and authorizations previously granted by another Member States*" could be reconsidered in order to define exactly under which specific conditions existing national registrations should be mutually recognised or endorsed by other Member States.
- Article 7 paragraph 1 of Directive 92/73 could be amended in order to increase the scope of products subject to a simplified registration procedure. In particular this could involve the explicit inclusion of other routes of administration and modifications/clarification concerning registerable dilutions.
- Article 7 paragraph 1 of Directive 92/74 could be amended in order to make the simplified registration procedure also applicable to homeopathics intended to be administered to food producing animals, whilst taking into account the importance of maintaining stringent measures to protect consumers in this sensitive area.
- Article 7 paragraph 2 of Directive 92/73 and 92/74 could be amended to allow for the use of fantasy names for combination preparations. The information required on the labelling: "*homeopathic medicinal product without approved therapeutic indication*" could be changed into "*homeopathic medicinal product without medical claim*". A possibility to include the normal daily dosage in the labelling and a revision of the warning to consult a doctor to make the labelling more consumer friendly could as well be considered.
- With regard to Article 9 paragraph 2 of Directives 92/73 and 92/74 (tests and clinical trials) it could be considered to make this provision binding and to demand explicitly that the "specific rules for tests and clinical trials in Member States" should provide for the involvement of appropriate experts in homeopathic and anthroposophic medicine.

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