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Dear Arielle

UK response to the 2nd draft of directive on traditional medicinal products

As requested at the April Pharmaceutical Committee I am submitting the UK's comments on the second draft of the traditional medicines directive.

We welcome the latest draft including a number of the specific improvements made. I enclose our detailed comments and would draw particular attention to the points we raise on:

- the strong case for appropriate recognition of non EU traditional medicines. We attach great importance to the need to recognize the culture of ethnic groups. We believe it should be possible to recognize medicines from other traditions without jeopardising safety
- the benefits of a European positive list to encourage harmonisation in relation to those traditional medicines in wide use across the EU *provided* it does not prevent Member States also drawing up additional positive lists to reflect their national markets and traditions and does not prevent applications being made in respect of products whose ingredients do not appear on such lists
- the need for further clarification of the relationship between traditional medicines registrations and 65/65/EEC authorisations.

I hope our comments are helpful.

Yours sincerely

R K Alder
Head of Executive Support

Comments on the second draft of the directive on traditional medicinal products

Article 1

1(1) We were not entirely surprised that the Commission reported to Pharmaceutical Committee that the specific suggestions from various Member States for extending the directive beyond herbals tended to be rather disparate and specific to the Member State concerned. This probably reflects variations between national markets as well as divergences in practices between Member States as to whether specific types products, such as fish oils, tend to be categorised as medicines. If there is insufficient common ground this may be an area where a degree of national flexibility may be realistic for an initial period.

1(2) We have concerns about the meaning and implications of the text which rules out products which “*can be authorised in accordance with article 3 of Directive 65/65/EEC*”. Arguably in some cases the only way of knowing whether an application for a medicinal product “can be” authorised under 65/65/EEC is if an actual application is first put in for that product. We are sure it would not be the intention of the directive to force companies to make speculative applications under 65/65/EEC. This suggests that it might be better to link any such provision restricting traditional medicines registrations more specifically to situations where two conditions both apply:

an identical or essentially similar product is authorised under 65/65/EEC in that Member State *and*

the product which is the subject of the application for a registration can be authorised under 65/65/EEC.

We reiterate a point made previously that it would be necessary to address the situation where a valid traditional medicines registration was granted and subsequently another company applied successfully under 65/65/EEC for an identical product.

If it is not possible to achieve a workable approach by following this line we would suggest reconsideration of the possibility of distinguishing between 65/65/EEC and traditional medicines registrations mainly by the information with the product.

1(2) We are still considering the reference to Article 7 of 92/73/EEC and will write again if we have points to make on this issue.

Article 2

2(1) We suggest for consideration that the words “*which consists exclusively of*” might be replaced by “*containing as active ingredients*”. There should perhaps also be an addition at the end of the paragraph “*whether or not in combination, in any of these cases, with one or more excipient*”

In Article 2(1) to 2(3) we suggest that “*substances*” might be replaced by “*drugs*” and “*herbal preparations*” might read “*herbal drug preparations*”.

Article 3

3(3)(c) We support the line which the Commission took at Pharmaceutical Committee that it was better to have a rolling period of time qualification for traditional use, e.g. 30 years, rather than to fix an inevitably arbitrary specific date.

3(3)(c) We suggest that “*bibliographic and expert evidence*” is replaced by “*expert, bibliographical or other evidence*”.

3(3)(c) We support the inclusion of the new sentence “*It is likewise satisfied if the number or quantity of ingredients of the medicinal product has been reduced during the period*”

3(3)(c) We suggest inserting after the first reference to “*corresponding medicinal product*” additional text along the lines of “*(or series of products comprising two or more corresponding medicinal products, or the medicinal product in question together with one or more such products)*”

3(3)(c)(i) We welcome the new words “*irrespective of the excipients used*”

3(4) We confirm our strong support for the principle of finding a way of regulating genuinely traditional medicines from non EU traditions. We think it is essential to recognize and respect the culture and traditions of ethnic groups. There are significant numbers of such products on the UK market, often used by specific ethnic groups. It is much preferable to be able to regulate them with strong emphasis on safety and quality than to force them into the grey or black market. It is likely that some of these products will have difficulty with the *safety* requirements (we think the new provisions of 3(3)(d) in particular and also of 3(3)(c) should enable regulators to protect public health). Likewise, the standards currently used to produce many of these medicines will need to improve substantially if they are to meet reasonable *quality* requirements. It would be entirely right to rule out specific medicines from registration where they fall short on safety or quality grounds. However, the problem will arise if regulators are required to rule out products on the basis that they do not satisfy a particular EU definition of *tradition*, whereas the specific medicine may be many centuries old. Ethnic groups and others who support the use of such products would be likely to regard such an approach as discriminatory.

The new suggestion of dealing with this problem by taking account of up to 15 years non EU usage provides some recognition of this issue. Inevitably, however, any figure of this kind for non EU usage is somewhat artificial if we are considering a medicine that is actually a thousand years old. The key issue is safety. One approach would be to allow Member States flexibility to accept some or all of the 30 years to be made up by non EU usage where they are satisfied that there is sufficient evidence effectively to assess safety. This could be helpful in allaying the fears of Member States concerned about pressure to accept applications where the products/ingredients were unfamiliar to orthodox science and safety was unclear.

Generally we would see a strong case for giving Member States a degree of flexibility in this area since the culture and experience of ethnic medicines is likely to vary very widely between Member States.

Article 4

4(3) The reference should be to article 14 rather than 16.

4(3) We suggest essential oils and possibly plant juices should be considered for inclusion in the category of simplified dossiers. We also suggest compliance with a monograph of the European Pharmacopoeia or the national pharmacopoeia of a Member State.

Articles 5 and 8

We are not clear on the relationship between the proposed positive lists mentioned in Articles 5 and 8. We cannot immediately see the case for *separate* positive lists of products and ingredients – if in fact this is the intention.

The main value we see in a positive list is that it could set parameters relating to ingredients, dosage and indications in order that applicants who make an application for registration of a specific product which falls within these parameters do not then need to demonstrate evidence of traditional use and safety. This approach would help to avoid unnecessary work on the part of both business and regulatory authorities. In this context we query whether it would better if Article 8 should refer to substances/ingredients rather than products.

As indicated in UK's comments at the Pharmaceutical Committee, we welcome the idea of a positive list established at European level which has the effect described above, *providing* it does not remove the possibility of individual Member States also preparing positive lists. It would be helpful if Article 8 of the Directive made specific provision to this effect.

We would have concerns, however, if the intention behind Article 5 was to set up a European list of specific substances permitted under the traditional medicines directive to the exclusion of substances not on that list. We assume that this is probably not the suggestion, but we think it would be difficult to manage such policy at either a national or EU level.

Article 7

7(c) We suggest this might read "*the product is harmful in the normal conditions of use*"

7(d) We have significant concerns about this provision. Applicants are not asked elsewhere in the Directive to demonstrate that the pharmacological effects or efficacy are plausible. On that basis it would seem difficult to introduce these as criteria relevant to a decision to refuse specific applications. Such a provision could also make it more difficult to draw up and apply clear guidelines – whether at European or national level – as to what constitutes acceptable evidence of traditional use.

7(f) We suggest “*external*” rather than “*cutaneous*” preparation. This is less restrictive on the basis that provision exists elsewhere in the directive to require data where necessary if, for example, there were concerns about excipients used in eye drops.

7(g) We would like to clarify the policy intention of this provision. Our earlier comments in relation to Article 5 and 8 are also relevant. This provision seems to be unduly restrictive if it means that an application will fail if the ingredients of the product are not on the Article 5 (or Article 8) list. We think it should be possible to gain registration by meeting the other requirements of the Directive even if the ingredients are not on the positive list(s).

Article 8

8(2)(c) We suggest it would be preferable if “specified strength read as “specified dosage”.

Article 10

We note that pharmacovigilance requirements are imported into this Directive by the cross reference to 75/319/EEC. In order to highlight the importance of this issue we would suggest that it may be desirable additionally to make an explicit reference to the requirements for adverse drug reaction reporting in this new Directive.

Article 11

We are content with the extended version of 1(a); but we have a suggestion concerning the wording in 11(1) “*contain a statement to the effect that*”. This does provide for useful national flexibility in an area where it might be difficult to reach an agreed view across Member States on a precise form of words. We would suggest for consideration that in addition to the existing material in 11(1) there should be a provision permitting individual Member States specifically to prescribe a set form of words consistent with the requirements of 11(1). There is a risk otherwise that there may be frequent and lengthy disputations with individual applicants wishing to test the boundaries of the law as to whether their proposed form of words complies with the requirement “*to the effect that*”.

Article 12

We think it may be feasible to shorten somewhat the amount of information required in an advertisement. One initial suggestion would be for a form of wording along the lines of “*a traditional medicinal product for use in [specified indication] for which efficacy has not been proven.*”

Article 14

We would welcome clarification of the proposed remit of the Committee, in particular in relation to Directive 99/83/EC.

Article 15

15(2) Given the complexity of the market we welcome the proposal for a significant transition period of 5 years.