Full list of questions put to the European Commission

1. Commissioner Dalli stated in a letter to Giles Chichester MEP on 13 April 2011 that 'herbal products falling under the definition of a medicinal product have to be authorised in accordance with the above mentioned rules (full marketing authorisation under Directive 2001/83/EC) until the adoption of Directive 2004/24/EC'. Given that no TCM or Ayurvedic products have yet to be registered under the traditional use registration scheme and that most are medicinal by function (Article 1.2(b), amending Directive 2004/27/EC), does this mean that such products may have been illegal in the EU prior to full implementation of Directive 2004/24/EC on 1 May 2011, and are most certainly illegal after this date?
2. When considering the 359 registrations granted EU-wide by the end of December 2010, the majority are for products which do not contain any whole-plant material and are based on alcohol- or acetone-extracted European single herbs, coming from the relatively recent (20th century) Germanic phytopharmaceutical tradition. Prior to 2004, many of the German products had already received national medicinal licences without undergoing the same quality-control systems as required for registration under Directive 2004/24/EC. It appears that the Traditional Herbal Medicines Products Directive (THMPD) was built around these German products, so they were THMPD-ready when the Directive was enacted. How can this be proportionate, from the perspective of Asian traditional medicines, when the latter undergo such different preparation and manufacturing methods that were not taken into account when the Directive's eligibility and technical criteria were developed?
3. Why has the Committee on Herbal Medicinal Products (HMPC) of the European Medicines Agency (EMA) reviewed so few herbal species associated with Chinese, Tibetan, Ayurvedic, Amazonian, African or other very long-established, non-European, healthcare traditions?
4. In some Member States, more and more products containing herbal

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ingredients that have in the past been sold as botanical food supplements are being deemed to be either unregistered medicinal products or unauthorised novel foods. This trend is primarily caused by competent authorities for medicines applying more scrutiny to botanical products, now that Directive 2004/24/EC is fully implemented. Where these products are based on long-standing, non-European traditions, they are generally incapable of accessing the THMPD registration system owing to eligibility, technical or cost challenges. Being unable to be sold any longer as food supplements, and effectively being 'locked out' of the THMPD regime, means they fall between regulatory regimes.

Does the Commission agree that such products are now illegal, and will it take steps to address this 'falling between two stools' problem?

5. Can the Commission envisage the establishment of a regulatory regime appropriate for non-medically qualified practitioners of holistic, long-standing traditions of medicine, who prescribe authentic traditional products?

   If so, when?

6. The Commission states in its experience report of 2008 (COM(2008)0584) that the registration procedure under Directive 2004/24/EC is 'not appropriate' for holistic traditions, such as those associated with Ayurveda and TCM, and that it might consider assessing the 'suitability of a separate legal framework for products of certain traditions.' Is the Commission prepared to progress its assessment of feasibility of such a framework?

7. Many multi-herbal, authentic traditional products from long-standing, non-European systems of medicine deal with multiple systems in the body. To date, the indications that have been accepted in those products that have been granted registration are generally limited to symptomatic relief of a single, minor condition. Will the Committee on Herbal Medicinal Products (HMPC) of the European Medicines Agency (EMA) accept authentic claims that involve multiple systems in the body, such as liver, lungs and spleen?

   Also, will claims be allowed that relate to metaphysical concepts that are fundamental to these traditions, such as 'chi' energy in traditional Chinese medicine or the three 'doshas' of Ayurveda?

8. Directive 2004/24/EC was intended to contain a full 7-year transition phase to allow sufficient time for companies to register products.

Why was the EMA's guidance on quality control requirements not prepared in advance of this transition period, rather than being altered during the course of it?

9. Consumer safety is cited as one of the major justifications for Directive 2002/24/EC. Many of the herbal products successfully gaining registrations are based on enriched extracts, produced by modern, non-traditional systems of extraction (e.g. alcohol, acetone, hydro-alcoholic, supercritical); however, the products themselves carry indications (medicinal claims) based on traditional preparations that are biochemically distinct or 'non-bioequivalent', such as watery decoctions.
   How can such a high degree of non-bioequivalence between herbal products and therapeutic indications guarantee public safety?
10. In a letter of 13 April 2004 to Giles Chichester MEP, Commissioner Dalli states:
    '….the simplified procedure does not reduce access to Chinese or Indian ayurveda medicinal products or of products of companies with reduced financial capacity…'
    The fact that so many traditional herbal medicines are comprised of decoctions of whole-plant material often derived from multiple herbal species – often more than 8 and sometimes more than 20 – creates a severe technical hurdle with regard to the EMA quality control guidelines. This is evidenced by the lack of applications from manufacturers of Chinese and Indian traditional medicines. Based on the EMA's figures up to December 2010, only 5% of the registrations granted involved products containing 5 or more herbal ingredients, and only 1% included products with more than 10 herbal ingredients. None of these were traditional Asian herbal medicines.
    Why has the Commission and the EMA not consulted with key manufacturers in the TCM, Tibetan and Ayurvedic sectors, all of which have long expressed grave concerns over the lack of suitability of the quality control procedures for complex polyherbal products based on traditional manufacturing methods?
    Also, why are so few of the herbs associated with these Asian systems of medicine subject to HMPC (Committee on Herbal Medicinal Products) monographs?
11. One of the primary ways in which Directive 2004/24/EC is intended to ensure that safe herbal medicinal products are placed on the market is by requiring pre-market authorisation of products that have undergone appropriate quality control testing. Among the most important tests are those that determine stability over a period of several months via an identified biomarker.
    How does the EMA ensure that sub-standard products have not been 'topped up' with, or adulterated by, the addition of a biomarker following the extraction phase?

12. The European Medicines Agency (EMA) guidelines on quality control continues to focus on tests that require identification of single biomarkers related to active constituents of individual herbs. This is in contrast with newer, more comprehensive analytical methods that characterise ('fingerprint') the full spectrum of chemical constituents, methods which are far more appropriate for polyherbal products based on comminuted herbs or watery decoctions that are associated with many of the major, non-European traditions.

    Why is the EMA so slow to recognise these full-spectrum analytical methods?

13. Many consumers have assumed that the 'Traditional Herbal Medicinal Products Directive' 2004/24/EC, as that title implies, provides a regulatory regime for products from the longest-standing traditions in herbal medicine, especially those associated with the great Asian traditions of Chinese and Ayurvedic medicine.

    Does the fact that a great many of the products registered to date contain synthetic polymers, synthetic preservatives and, in some cases, artificial colours and flavours, not suggest there is a problem with the eligibility requirements, given that such products cannot properly be regarded as 'traditional'?

14. It is clear from the legislative history of Directive 2004/24/EC that a major stimulus for the Directive's development came from the poisonings associated with a Brussels-based slimming clinic, operated by medical doctors, in 1990. Of the 135 patients who contracted moderate- to late-stage kidney disease, which predisposed them to urothelial cancer, all were prescribed slimming pills including both synthetic drugs and herbal products within a three-month period. The case is widely considered the worst known case of herbal poisoning and has been attributed to aristolochic acids derived from a Chinese herb, aristolochia fangchi. However, three court cases brought by victims who consumed the slimming pills have failed to establish causation by aristolochic acids. Nonetheless, the Directive was presented as a means to ensure consumers were protected from unsafe herbal medicines, with the aim of ensuring that such an event would not be repeated.

    Given that not a single Chinese herbal product has yet been registered under the Directive, how are consumers being adequately protected? And is it not the case that medical doctors are exempted anyway under Article 5(1) of Directive 2001/83/EC and so are allowed to prescribe unregistered medicines, meaning there is still no additional safeguard protecting consumers from a repeat of the 1990 event?

15. Does the Commission and the EMA recognise that it is possible for an herbal ingredient or substance to trigger a significant metabolic or immunological response, indirectly, rather than directly? (This is generally because the product provides a factor or substrate that is in inadequate supply in the diet and so enhances specific metabolic pathways.) In such cases, is it fitting that such products should be deemed medicinal by function, according to the definition in Article 1.2(b) of amending Directive 2004/27/EC, when effectively these products are simply enhancing homeostatic mechanisms? (It should be recognized that many 'healthy foods', such as broccoli, berry fruits and oily fish, operate in exactly this way.)
16. What was the justification for including the words 'immunological or metabolic action' in the 2004 amendment of the European medicinal code (Article 1(1) of Directive 2004/27/EC), as this amendment effectively makes all beneficial herbal products medicinal by function? (The amendment was not supported by the European Parliament at second reading.)
17. At present, some Member States' competent authorities are unnecessarily medicalising herbs, and products containing herbs, that have an excellent safety profile and history of safe use.

    Would the European Medicines Agency consider a categorisation system for individual herbal species and preparations to allow more equitable delineation of the food/medicine borderline by Member States' competent authorities?
18. The claimed indications currently allowed for products registered under Directive 2004/24/EC (amending, as regards traditional herbal medicinal products, Directive 2001/83/EC on the Community code relating to medicinal products for human use) are restricted to minor and self-limiting conditions.

    What is the legal basis of the decision to exclude indications for more serious conditions, such as Type 2 diabetes and osteoporosis, which have become a scourge in modern, western societies and for which Asian systems of traditional medicine have particularly effective solutions?

    Is it assumed that serious diseases need to be treated with more hazardous products? Is this territory reserved for conventional pharmaceuticals that have undergone full marketing authorisation procedures? Or are there other reasons?
19. What is the Commission's policy on the use of herbs that have a history of medicinal use in botanical food supplements? If an herb is successfully registered under the

THMPD scheme, may it still, under specific conditions, be sold within a food supplement?

20. The typical cost for registration for the above medicines, including fees and quality control testing is in the order of EUR 200 000 per product. Given that a typical supplier of traditional, non-European herbal medicines is generally required to carry a line of a least 100 products, the cost of registering these would amount to around EUR 20 million. If these products each generated an annual revenue of EUR 5000, it would take 40 years to recover the initial costs of registration.
    What impact assessment has the European Commission undertaken to evaluate these kinds of potential cost burden on typical SMEs engaged in the supply of products associated with non-European systems of medicine?
21. Many products associated with long-standing, non-European systems of medicine contain non-herbal active ingredients, such as minerals.
    Why have such products been excluded from Directive 2004/24/EC?
    Also, considering the views expressed by the Commission in its experience report COM(2008)0584, will the Commission be addressing this issue and supporting amendment of the directive to make products containing non-herbal ingredients potentially eligible?
22. Why does Directive 2004/24/EC require 15 years usage of herbal products within the EU as a component of the 30 years traditional use requirement? Why is it unsatisfactory to provide evidence only from outside the EU where, in some cases, there are hundreds of years of verified usage for particular classical formulae?
23. The traditional use requirement in Directive 2004/24/EC appears to have no flexibility with regard to the specific combination and ratio of herbs. If there is a minor adjustment to a formulation of a product that met the 15/30 year use requirement to cater for different target groups or more recent science, the product would presently not be deemed eligible to the scheme.
    Will the Commission consider the possibility of allowing more flexibility in 'corresponding products' eligible to the traditional use requirement in the future?