



## **Briefing note: sources of evidence of traditional use under the proposed Directive on Traditional Herbal Medicinal Products.**

### What are the requirements to demonstrate traditional use of a remedy?

1. Under the proposed Directive on Traditional Herbal Medicinal Products applicants are required to produce bibliographic or expert evidence of traditional use. In summary, the medicinal product in question or corresponding products(s) should have been in medicinal use throughout a period of at least 30 years preceding the date of application. At least 15 of the 30 years use must relate to the European Union.
2. A corresponding product is characterised by having the same active ingredients (but not necessarily the same excipients); the same or similar intended purpose, equivalent strength and posology and the same or similar route of administration.
3. The requirement to show medicinal use for 30 years can be satisfied where the number or quantity of ingredients has been reduced during the period.
4. The requirement to demonstrate traditional use is lifted where the product complies with the European positive list that would be established by the Committee on Herbal Medicinal Products.

### What sources of evidence of traditional usage may be used?

5. The following are *examples* of sources of information that applicants could consider using:
  - any published information referring to specific product formulations eg. old editions: Martindale: *List of Preparations*; German Rote List; Potter's New Cyclopaedia etc
  - company archive materials: brochures, sales lists, invoices etc
  - use of licensed herbal medicines in UK or other Member States
  - other bibliographic evidence, eg text books, pharmacopoeia
  - lists of traditionally used herbs currently in use in other Member States (e.g. German, French, others)
  - documentation relating to herbal medicines manufactured as "specials"
  - evidence from herbal practitioners.

Is it permissible to refer to the evidence of products on the UK market that are not currently classified as medicines for the purpose of compiling evidence of traditional use for an application for registration?

6. The key requirement in the Directive is that the medicinal product in question or a corresponding product “has been in medicinal use throughout a period of at least thirty years preceding the date of application, including at least 15 years within the Community”. The MHRA does not rule out the possibility that an applicant might be able to demonstrate that a product, sold legally under a regulatory regime other than medicines, nonetheless had in practice a significant pattern of medicinal use. Many products are close to the borderline between medicines and other regulatory categories and therefore the MHRA would wish to look case by case at the evidence provided by applicants. This might well be an area where an applicant wished or needed to deploy evidence from more than one source.

If a product is legally sold under another regulatory regime but a company nonetheless wishes to obtain a traditional use registration, can the company strengthen evidence of traditional use by turning its existing product into a medicinal product, e.g. sold under Section 12(2) of the Medicines Act 1968? Would such a change mean that the product was no longer covered by transitional protection?

7. Several issues arise in this situation as to whether such an action would have an impact on transitional protection. They include the date at which the change in the product was made relative to 30 April 2004, 30 October 2005 and 30 April 2011 (A, B and C days), and whether the change would be such as to in effect create a different product, ie one which was not able to benefit from transitional protection. Applicants may find it helpful to refer to MHRA guidance on these issues. However, where it is clear that there has been a product on the market for the requisition period but that the issue is over the evidence of medicinal use, MHRA’s advice would be for applicants to avoid complicated manoeuvres of the kind predicted in the question. It would be more effective to concentrate efforts on identifying reasonable evidence that the product in question, or others that could be regarded as corresponding products, had traditionally had medicinal use. Any potential applicants facing this issue may also find it helpful to raise the point with MHRA when they have reached the position of having identified their proposed registrations and the evidence they have available to support traditional usage.

Can evidence from overseas departments or territories be used to satisfy the requirement to demonstrate usage within the EU?

8. Areas classified as "*Outermost regions*" are an inherent part of the European Union. Evidence from these areas would be regarded as evidence of usage within the EU. These are: Guyane, Guadeloupe, Martinique and Reunion (French Overseas Departments); Azores and Madeira (Portugal); and Canary Islands (Spain).
9. In contrast, *Overseas Countries and Territories* that have special relations with individual EU Member States are not part of the EU. There is a longer list of such territories including: French Polynesia, Netherlands Antilles, Cayman Islands, and St Helena. The usage in countries on this list can not be used as evidence of traditional use.

## Pointers as to the use of evidence

10. At this early stage it may be helpful to give some pointers. These may need to be supplemented as preparations for the Directive continue:

- where a source that is clearly recognised as authoritative within a particular herbal tradition indicates there is an significant pattern of traditional use which, in context, meets the requirements of the Directive, a single source of evidence of traditional use may well often be sufficient
- such an authoritative source might be an authoritative written document, such as a textbook that was up-to-date. However, it could also be a herbal expert who is generally recognised within the tradition as having expertise on the wider use of herbal remedies, and not simply their own practice (e.g. by virtue of academic work or recognised expertise in a professional organisation)
- where a source of evidence is potentially narrower in scope – e.g. from an individual herbalist or pharmacist only able to talk knowledgeably about their own practice rather than bringing to bear authoritative knowledge about the wider picture, it may well be necessary for the applicant to bring together more than one source in order to demonstrate that there has been continuous use
- where an applicant wishes to refer to evidence from practising herbal practitioner(s) the MHRA would expect that such practitioner(s) would belong to an appropriate professional body
- in the case of a company referring to its sales records, depending on the length and scale of their activities, it may be possible reasonably to infer the required period of use is satisfied from this single source
- where applicants are supplying specific records of actual use it will *not* be necessary to supply specific records, e.g. sales records, relating to each and every month over the 30 year period. The MHRA is content to consider on the merits of the case reasonable arguments from applicants that it is feasible to make a sensible extrapolation from evidence available
- inclusion of an item on positive lists of traditional use that exist in certain other Member States under their existing regulatory schemes is not of itself *direct* evidence that corresponding medicinal products have been in continuous use in that country so as to meet the requirements of the Directive. However, in many cases it may well be strongly indicative that this is likely to be so. While it is not the MHRA's responsibility under the Directive to research traditional use, the Agency intends to raise the general issue in the existing Herbal Medicinal Products Working Party at the EMEA (or the successor Committee under the Directive) to see if there are any further pointers that can be given about the use of such lists as evidence of traditional use. The MHRA will also press the Working Party/Committee to assemble such existing lists in English so that they can be more readily accessed

- it will often be convenient or necessary for applicants to use several sources of evidence in order to complete the evidence required. For example:
  - in the case of traditional combinations of active herbal ingredients, while the traditional use of individual ingredients may be well documented in text books etc, there may be a particular role for expert herbalists in giving testimony about the use in that herbal tradition of that specific herbal combination
  - if an applicant is making reference to unlicensed remedies on the market under Section 12 of the Medicines Act 1968, since these are sold without written indications, it would not be possible to rely simply on evidence of the existence of such products on the market. In order to meet the requirement that there are corresponding product(s) with the same or similar intended purpose it would be necessary also to refer to other source(s) of evidence for appropriate traditional indication(s) for that remedy. For example, there could be evidence from text books or qualified practitioners might be able to testify on the basis of their usage of S12(1) remedies.