Guidance on Sources of Evidence of Traditional Use for applications for Traditional Herbal Medicinal Products

What are the requirements to demonstrate traditional use of a herbal medicinal product?

1. Under the Traditional Herbal Registration Scheme for 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.
   - **For products intended to be marketed in the whole of the UK or Northern Ireland only**, at least 15 years of the 30 years use, must relate to use in the EU/EEA.

   - **For products intended to be marketed in Great Britain only**, the MHRA may be able to accept the 15 years of traditional evidence from a wider range of countries in addition to the UK and EU/EEA countries.
     Suitable countries will be those that have a level of pharmacovigilance equivalent to that of the UK. This is to ensure that any safety issues have been properly identified to support the traditional use of the product. The MHRA will publish a list of suitable countries for this purpose on the gov.uk website and update this list as new entries arise.

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. a) **For products intended to be marketed in the whole of the UK or Northern Ireland only:** The European Union list (formerly known as the Community List) developed by the European Union (EU) Committee on Herbal Medicinal Products (HMPC) can be used to demonstrate traditional use and safety when the product complies with the relevant entry. In these cases, applicants are strongly encouraged to contact the MHRA at an early stage, using our pre-application notification scheme. This provides an early opportunity for the MHRA to discuss any issues with the applicant.

   b) **For products intended to be marketed in Great Britain only:** The European Union list (formerly known as the Community List) developed by the European Union (EU) Committee on Herbal Medicinal Products (HMPC) can be used to help support evidence of traditional use and safety.
   The MHRA may produce its own list of herbal substances, preparations and combinations which will include entries from the existing EU list and will be updated as new entries arise. The MHRA list can be used to demonstrate traditional use and safety when the product complies with the relevant entry. In these cases, applicants are strongly encouraged to contact the MHRA at an early stage, using our pre-application notification scheme. This provides an early opportunity for the MHRA to discuss any issues with the applicant.

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 e.g. Old editions: Martindale: List of Preparations; German Rote List; Potter's New Cyclopaedia etc
   - company archive materials: brochures, sales lists, invoices etc
   - for products to be marketed in the whole of the UK or Northern Ireland only, use of licensed herbal medicines within the EU/EEA
   - for products to be marketed in Great Britain only, use of licensed herbal medicines within the UK, EU/EEA or wider range of countries. Suitable countries will be those that have a level of pharmacovigilance equivalent to the UK to ensure that any safety issues have been properly identified to support the traditional use of the product. The MHRA will publish a list of suitable countries for this purpose on the gov.uk website and update this list as new entries arise.
   - other bibliographic evidence, e.g. text books, pharmacopoeia
   - documentation relating to herbal medicines including those supplied by herbal practitioners

When preparing an application for a traditional herbal registration, can an applicant refer to European Union (EU) herbal monographs prepared by the Committee on Herbal Medicinal Products (HMPC) in order to demonstrate safety and traditional use?

6. EU herbal monographs published by the HMPC and their associated assessment report can be used to help support safety and traditional use. In cases where the associated assessment report is relied upon as evidence to demonstrate the traditional use and safety of the product, applicants are strongly encouraged to contact the MHRA at an early stage, using our pre-application notification scheme. This provides an early opportunity for the MHRA to discuss any issues with the applicant.

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?

7. The key requirement of the Traditional Herbal Registration Scheme 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 either of the following depending on whether the product will be marketed in the whole of the UK, Northern Ireland only or Great Britain only:
   - **For products intended to be marketed in the whole of the UK or Northern Ireland only**, at least 15 years of the 30 years use, must relate to use in the EU/EEA.

   - **For products intended to be marketed in Great Britain only**, the MHRA may be able to accept the 15 years of traditional evidence from a wider range of countries in addition to the UK and EU/EEA countries.
     Suitable countries will be those that have a level of pharmacovigilance equivalent to that of the UK. This is to ensure that any safety issues have been properly identified to support the traditional use of the product. The MHRA will publish a list of suitable countries for this purpose on the gov.uk website and update this list as new entries arise.

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.

Can evidence from overseas departments or territories be used to satisfy the requirement to demonstrate usage within the whole of the United Kingdom, Northern Ireland only and Great Britain only?

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 and thereby considered suitable. 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 cannot be used as evidence of traditional use.

Pointers as to the use of evidence

10. The following pointers may be helpful:

- where a source that is clearly recognised as authoritative within a particular herbal tradition indicates there is a significant pattern of traditional use which, in context, meets the requirements of the Traditional Herbal Registration Scheme, 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 countries 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 Traditional Herbal Registration Scheme. However, in many cases it may well be strongly indicative that this is likely to be so

- 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