

**Reforms of s12(1) of the Medicines Act 1968: the regulation of unlicensed herbal medicines commissioned by a registered practitioner from a third party to meet the needs of individual patients**

Introduction

1. This informal discussion paper is one of a series prepared by the Medicines and Healthcare products Regulatory Agency (MHRA) which explores possible reforms of section 12(1) of the Medicines Act 1968 and its associated provisions. S12(1) is the legislative provision used by herbal practitioners, and some others, carrying out a business in which they prepare unlicensed herbal medicines to meet the individual needs of patients identified in consultation.
2. This specific paper explores ideas for reforming the regulation of unlicensed herbal medicines commissioned by herbal practitioners from a 3<sup>rd</sup> party to meet the special needs of individual patients identified in face to face consultation. The paper is drafted on the assumption that work on the statutory regulation of the herbal medicine profession will lead in due course to the creation of a defined body of herbal practitioners that can be identified in law. In the text we have sought to indicate those areas where there are particular legal constraints on the direction of reform. Ideas for discussion and comment are set out at para 14 onwards. The MHRA welcomes dialogue with interested parties on these ideas. The paper is intended to help focus such discussions. The MHRA's expectation is that this work will help to pave the way for a subsequent formal public consultation.

Background

3. Alongside DH-led work on the statutory regulation of the herbal medicine profession the MHRA has pursued related reforms of the medicines regime which is currently set out in section 12(1) of the Medicines Act 1968. These are the provisions that allow practitioners to make up unlicensed herbal remedies to meet the individual needs of patients identified in face to face consultation.
4. One important feature of the possible reforms is possible future arrangements that would permit registered herbal practitioners, recognised as authorised healthcare professionals for the purposes of relevant European medicines legislation, to commission a 3<sup>rd</sup> party to manufacture an unlicensed herbal medicine to meet the special needs of an individual patient.

The use of unlicensed herbal medicines commissioned by herbalists from a 3<sup>rd</sup> party

5. The MHRA is aware that in a number of traditions, notably traditional Chinese and Ayurvedic medicine – but also western herbalism - significant use is made of herbal medicines commissioned by the herbal practitioner from a 3<sup>rd</sup> party.

Some of these medicines are of a nature and complexity such that it would not be realistic for a practitioner to manufacture them him/herself. In principle the MHRA would wish to accommodate this practice by registered practitioners within an updated regime, providing important requirements are met.

### Objectives

6. The MHRA considers that any updated arrangements must:
  - provide necessary public health protection in an area of known risk
  - be legally robust
  - give due regard to issues of regulatory impact.

### Public health issues

7. Currently the use of manufactured remedies intended for practitioner supply is one of the greatest areas of public health risk with unlicensed herbal medicines. There have been repeated examples found of unlicensed medicines recovered from traditional Chinese medicine clinics that have illegally contained toxic or potent ingredients such as high levels of heavy metals or undeclared pharmaceuticals, also ingredients such as human placenta or animal excreta that pose a variety of public health risks. Ayurvedic products have also been found to contain heavy metals or arsenic.
8. These examples in MHRA's view are indicative, variously, of:
  - internationally variable manufacturing standards, sometimes falling well below levels that would be acceptable for Good Manufacturing Practice (GMP) in the EC
  - lack of security and assurance in the supply chain
  - cultural issues, as in manufacturers or practitioners not recognising or accepting that some practices, such as the inclusion of heavy metals in unlicensed herbal medicines, even though they may be part of certain traditional medicines systems, are not legal in the UK
  - deliberate deception of the public, as in products illegally containing pharmaceuticals that are passed off as "herbal" or "natural"
  - weak regulation combined with lack of a comprehensive and enforceable code requiring all herbal practitioners to follow a professional approach that rules out the purchase of products and ingredients from unreliable sources.

### Legal parameters for a new scheme for commissioning unlicensed herbal medicines from a 3<sup>rd</sup> party

9. The MHRA's view is that, in contrast to herbal remedies prepared by a practitioner, herbal medicines commissioned from a 3<sup>rd</sup> party will generally be "prepared industrially or manufactured by a method involving an industrial process." This is because such remedies are typically produced using relatively sophisticated industrial processes.

10. Under Directive 2001/83/EC, as amended, industrially produced herbal medicinal products require either a marketing authorisation (MA) or a traditional herbal registration (THR). However, under Article 5 *“A Member State may, in accordance with legislation in force and to fulfil special needs, exclude from the provisions of this Directive medicinal products supplied in response to a bona fide unsolicited order, formulated in accordance with the specifications of an authorized health care professional and for use by an individual patient under his direct personal responsibility.”*
11. In MHRA’s view it may be possible to regard registered herbal practitioners, following statutory regulation of the profession, as authorised healthcare professionals for the purposes of Article 5. Practitioners who follow agreed professional standards as a consequence of voluntary membership of a professional association clearly would not come within the terms of Article 5.
12. Any updated scheme for registered herbalists to commission unlicensed herbal medicines from a 3<sup>rd</sup> party must be constructed so as to comply fully with the requirements of Article 5, otherwise it will not be legally sustainable.

The existing “Specials” scheme used by doctors

13. By way of information and comparison, a summary of the existing “Specials” scheme is attached at Annex A.

Ideas for discussion on arrangements for registered herbalists to commission unlicensed herbal medicines from a 3<sup>rd</sup> party

14. The following sections (A – F) present ideas for discussion.
15. The position as regards the use of these arrangements by any other statutorily regulated healthcare professionals who supply unlicensed herbal medicines to meet the special needs of individual patients following one to one consultation would need to be considered in the light of developments on professional regulation.
16. Full details of the EC Guide to Good Manufacturing Practice (GMP) can be found at <http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/homev4.htm>.
17. As any implementation of the kind of scheme floated in this paper may be some years away, further work on the issue will also need to take account of any wider policy or legal developments in the intervening period relating to the use of Article 5 of Directive 2001/83/EC.

### *A. Meeting the special needs of individual patients*

- *The activity must be practitioner driven to meet the needs of individual patients, and not a covert way to avoid the requirements for an MA or a THR.*
- *Therefore, it should not be permitted for manufacturers, importers or wholesale dealers to advertise or market specific products to herbal practitioners.*
- *It should also not be permitted for manufacturers, importers, wholesale dealers or practitioners to advertise these unlicensed products to the public.*
- *It should, however, be possible for manufacturers, importers or wholesale dealers of these unlicensed products to advertise to practitioners that they can provide a service of supplying these unlicensed herbal medicines (in accordance with the parameters of the scheme).*
- *It should not be permitted for a practitioner to commission an unlicensed herbal medicine under this scheme where there is an existing suitable product with a THR or an MA.*
- *However, the above point is qualified as follows: it should be recognised that a patient's personal preference for herbal medicine can constitute a special need. Therefore, the fact that there is a conventional, non herbal, medicinal product with an MA should not itself be a bar to the application of the proposed scheme.*
- *The purchaser should specify to, or agree with, the manufacturer or assembler the qualitative and quantitative specification of the product required (unless the purchaser is a wholesaler in which case there would need to be a clear communication through the wholesale chain of the requirements).*
- *Stocks of unlicensed herbal medicines may be prepared in advance, eg experience can be used to anticipate demand. Levels held should be consistent with the purpose of the scheme.*
- *Wholesalers may hold a stock of specials in anticipation of orders.*
- *In the scheme that applies in conventional medicine there is a limit on the stocks to be held by the practitioner. This helps to ensure that such medicines are genuinely being used for special needs.*
- *Such limits may be inappropriate for herbal medicine, where the significant use of practitioner commissioned medicines is likely to be integral to the activity of some registered herbal practitioners (eg in TCM and Ayurveda).*
- *However, the absence of limits would only be possible if the scheme overall complied with the requirements of article 5 of Directive 2001/83/EC (see para 10 above). Other elements of the scheme might need to be adjusted accordingly.*

***B. What ingredients would be permitted for use under this scheme?***

- *There should be a positive list of permitted herbal ingredients/classes of ingredients for which it was not necessary for the licence holder (see section C below) to notify MHRA in advance of an intention to supply.*
- *There should be a negative list of ingredients/classes of ingredients that are explicitly excluded from this scheme.*
- *In any other cases there should be a requirement for the relevant licence holder to notify the MHRA in advance of the supply of the unlicensed herbal medicine and the MHRA would have a period (eg of X days) within which it would have the opportunity to object to the supply.*
- *The profession would have the opportunity to propose items for inclusion in the lists. The MHRA would seek the advice of the Herbal Medicines Advisory Committee on the positive list and negative lists.*
- *In principle a limited range of non herbal ingredients used in traditional medicines could be permitted for inclusion on the positive list; however, this would be subject to full assessment on public health grounds, which would include not only issues inherent to the ingredient and its use, but also an assessment of potential safety issues arising from quality (for example in relation to TSE and transmission of viruses).*

***C. What licensing requirements would apply to manufacturers, importers, wholesale dealers?***

- *Manufacturers in the UK would be required to hold a special manufacturer's licence permitting the manufacture of these unlicensed products. To get a licence standards of GMP would have to be demonstrated.*
- *Importers of products from a third country would be required to hold a manufacturer's (importers) licence. This means that practitioners would not be able to import these products themselves, unless they held a manufacturer's (importers) licence. (MHRA notes that on a number of occasions when unsafe products have been identified in clinics it has transpired that practitioners may have directly or indirectly procured supplies from unsafe sources, such as relatives abroad).*
- *Importers should not use overseas manufacturers that follow standards below those equivalent to European GMP .*
- *Wholesale dealers would be required to hold a wholesale dealers licence for the procurement and distribution of the product within the EU.*
- *Individual practitioners commissioning an unlicensed product directly from a manufacturer based in the EU would similarly be required to hold a wholesale dealer's licence.*
- *These licence holders would need to comply with the conditions of their licence, the requirements of The Unlicensed Medicinal Products for Human Use (Transmissible Spongiform Encephalopathies) (Safety) Regulations 2003 and all relevant requirements of the scheme described in this paper, eg no advertising of specific products, the requirement to notify the MHRA etc.*
- *MHRA would inspect these various licence holders in the normal way.*
- *There would be a requirement for detailed record keeping by these licence holders as well as by practitioners and these would be subject to inspection/enforcement by the licensing authority. This would enable recall of products, also MHRA would be able to check compliance with the terms of the scheme. Records to be kept available to the licensing authority would include those relating to manufacture and/or assembly, importation, any relevant testing, and sale or supply.*
- *In view of known public health risks, the audit by MHRA of importers would include a strong focus on what steps the importer had taken to assure themselves of the quality and safety of imported medicines.*
- *The MHRA would have the power to require the importer to have imported products tested eg for the presence of heavy metals. (This is not intended as a substitute for the importer ensuring that the overseas manufacturer had systematic quality controls).*

***D. How is it envisaged that Good Manufacturing Practice requirements would apply?***

- *The manufacture and/or assembly of the unlicensed products must be carried out under such conditions as to ensure that the product is of the qualitative and quantitative specifications required by the customer.*
- *The product must comply with any relevant monograph of the EP or BP.*
- *Other than when a product is required for the immediate use (eg before standard tests can be completed and not for stockholding) of a single patient or a small number of patients, QC testing on each batch should be the same as performed on comparable registered or licensed products. Views would be welcome on what kind of testing should be performed or other assessment in circumstances where testing is not feasible.*
- *When required for the immediate use of a single patient, generally the following minimum controls should be applied:*
  - *all raw materials should have an adequate assurance of freedom from TSE risk*
  - *there should be an assurance that any raw materials that are subject to a BP/EP monograph are in compliance*
  - *confirmation of identity*
  - *traceability.*
- *Licensed or registered herbal medicinal products used as ingredients do not need to be tested.*
- *As applicable, the specification of the product should include QC tests to be carried out.*
- *Where stockholding is routine, stability data should be available to justify the shelf life.*

***E. How will it be possible to identify manufacturers that can supply these unlicensed herbal medicines made under GMP conditions?***

- *The MHRA puts forward the proposition that it would not be consistent with registered herbal practitioners' professional status if they were using medicines procured from manufacturers where there is no reliable assurance that standards equivalent to EU GMP are being followed.*
- *Many products made up for herbalists are likely to be complex and multi ingredient. Once the product is manufactured it would not be possible for a third party, eg an importer or practitioner, to determine what was in the product. This underlines the critical importance that the manufacturer is operating to assured GMP standards and that compliance with these standards is regularly audited.*
- *UK manufacturers of these products will be required to hold a special manufacturer's licence in the UK and therefore will be readily identifiable.*
- *There will be a range of other manufacturers in the EU who hold a manufacturer's licence for herbal medicines with a marketing authorisation or traditional herbal registration and therefore are likely to be able to make these unlicensed herbal medicines for practitioners to high standards, (if they choose to operate in this part of the market).*
- *It is likely that there will progressively be a number of overseas sites which manufacture registered traditional herbal medicines; these manufacturers will have demonstrated high standards and might therefore be a suitable choice for manufacture of these unlicensed practitioner products; however, it is uncertain how many traditional Chinese or Ayurvedic products will be registered under Directive – and when - given the proportion of medicines intended for practitioner only supply in response to individual needs in these traditions.*
- *Overseas manufacturers that meet their own national GMP standards will not necessarily operate to standards equivalent to those regarded as acceptable in the EU – such standards, and their enforcement, may vary widely. They may also be affected by cultural differences, eg over the acceptability of including heavy metals in unlicensed traditional medicines.*
- *If a site, eg an overseas one, is not already operating to the necessary standards it must be very doubtful in many cases whether the size of the UK market in unlicensed manufactured practitioner medicines would be such as to create a significant incentive to invest in standards. It must also be doubtful whether an importer would have sufficient leverage to require the manufacturer to improve standards.*
- *Taking TCM as an example, there is persistent evidence of erratic and unreliable standards in imported manufactured unlicensed herbal medicines intended for practitioner use. The MHRA would wish to ask what steps would the herbal sector envisage to ensure that unlicensed TCM herbal medicines would consistently be of acceptable standards, consistently containing the stated, legal ingredients, and free from contamination and adulteration?*

#### *F. Other issues*

- *Various other features of medicines regulation would need to apply*
  - *adverse reaction reporting*
  - *patient information provisions*
  - *sanctions (up to and including the loss of licences).*
- *The position as regards the use of these arrangements by any other statutorily regulated healthcare professionals who supply unlicensed herbal medicines to meet the special needs of individual patients following one to one consultation would need to be considered in the light of developments on professional regulation.*
- *As proposals develop, other issues will need careful consideration in order to ensure the overall coherence of regulatory arrangements, including how the scheme will tie in with the existing specials scheme. For example, should the arrangements discussed in this paper apply to all herbal medicinal products, or only to products which would otherwise be required to obtain a traditional registration? How should products with non herbal ingredients be treated?*

**UNLICENSED MEDICINES – “SPECIALS”**

- Medicines legislation (The Medicines for Human Use (Marketing Authorisations Etc.) Regulations 1994/SI 3144) requires that medicinal products are licensed before they are marketed in the UK. However, Schedule 1 to those Regulations sets out a number of exceptions to that principle.
- Some patients may have special clinical needs that cannot be met by licensed medicinal products. So that these special needs may be met, the law allows manufacture, importation and supply of unlicensed medicinal products (commonly known as "specials") subject to certain conditions.
- The conditions are that there is a bona fide unsolicited order, the product is formulated in accordance with the requirement of a doctor or dentist registered in the UK, and the product is for use by their individual patients on their direct personal responsibility.
- A practitioner may prepare or procure a “special” for administration to one or more of his own patients. The amount of stock held per practitioner is limited to a total of 5 litres of fluids or 2.5 kilograms (such as tablets or capsules) of “specials” products.
- An unlicensed relevant medicinal product may only be imported in accordance with the Medicines for Human Use (Manufacturing, Wholesale Dealing and Miscellaneous Amendments) Regulations 2005.
- An importer must hold the appropriate wholesale dealer's or manufacturer's (import) licence and must comply with their licence conditions.
- Importers` licence conditions include the requirement that they must notify the MHRA on each occasion that they intend to import such a product.
- Only small quantities may be imported under each notification - no more than 25 single doses or an amount sufficient for 25 courses of treatment not exceeding 3 months.
- Importation may proceed unless the importer has been informed by the MHRA within 28 days that it objects to importation. (The MHRA may object and prevent importation because it has concerns about the safety or quality of the product, or because there is an equivalent licensed medicinal product available and it is not satisfied that there is a "special need" for the supply to an individual patient).