

**EXPLANATORY MEMORANDUM TO THE
MEDICINES (TRADITIONAL HERBAL MEDICINAL PRODUCTS FOR
HUMAN USE) REGULATIONS 2005**

2005 No. 2750

1. This explanatory memorandum has been prepared by the Medicines and Healthcare products Regulatory Agency (MHRA) and is laid before Parliament by Command of Her Majesty.
2. **Description**
 - 2.1 These Regulations transpose into UK legislation Directive 2004/24/EC. Directive 2004/24/EC amends the principal Directive regulating the marketing of medicinal products in the European Community (Directive 2001/83/EC) to introduce a requirement for each EU Member State to establish a registration scheme for manufactured traditional herbal medicinal products. This registration scheme constitutes a simplified version of the requirements that normally apply for an industrially produced medicine to be placed on the EU market.
3. **Matters of special interest to the Joint Committee on Statutory Instruments**
 - 3.1 None
4. **Legislative Background**
 - 4.1 Directive 2004/24/EC of the European Parliament and of the European Council of 31 March 2004 amends, as regards traditional herbal medicinal products, Directive 2001/83/EC on the Community code relating to medicinal products for human use. This instrument, made under section 2(2) of the European Communities Act 1972, transposes the majority of provisions of Directive 2004/24/EC.
 - 4.2 This Memorandum should be read in conjunction with a number of other Regulations. The Medicines (Advertising and Miscellaneous Amendments) Regulations 2005 implement the requirements of Directive 2004/24/EC as they affect the advertising of traditional herbal medicinal products. The provisions of Directive 2004/24/EC relating to manufacture and wholesale dealing of traditional herbal medicinal products are implemented by the Medicines for Human Use (Manufacturers, Wholesale Dealers and Miscellaneous Amendments) Regulations 2005. The Medicines for Human Use (Marketing Authorisations etc) Amendment Regulations 2005 disapply parts of the Marketing Authorisation Regulations in relation to traditional herbal products in order to achieve the intended effects of Directive 2004/24/EC.
 - 4.3 The Medicines for Human Use (Fees Amendments) Regulations 2005 set fees applicable to the registration scheme to be introduced under Directive 2004/24/EC.
 - 4.4 A Transposition Note is attached.

4.5 The approach taken to transposition has been to cross-refer to the provisions of Directive 2001/83/EC. The Directive, and in particular the Annex to the Directive, is lengthy and contains technical details, and the Regulations are not aimed at the general public. The Regulations avoid “gold plating” or “double banking” of the Directive’s provisions.

4.6 The proposals were cleared by the House of Lords EU Scrutiny Committee in March 2002. The proposals were cleared by the House of Commons EU Scrutiny Committee, following a Standing Committee debate in June 2002, in September 2003.

5. Extent

5.1 These Regulations apply to all of the United Kingdom.

6. European Convention on Human Rights

6.1 No statement required.

7. Policy background

7.1 The policy objective of Directive 2004/24/EC is to promote harmonisation within the European Union and to assure consumers of public health protection in relation to traditional herbal medicinal products.

7.2 In principle, traditional herbal medicinal products were already covered by the Community code relating to medicinal products for human use, as set out in Directive 2001/83/EC. However, in practice it was widely recognised across the EU that it was not always realistic or practicable for applicants to obtain a marketing authorisation, and in particular on account of the difficulty of meeting the requirement to demonstrate the efficacy of the product. Various EU Member States had adopted a range of pragmatic measures to allow traditional herbal medicines to remain on national markets. These measures inhibited the development of the market and in some cases gave insufficient protection to public health.

7.3 To address this situation, Directive 2004/24/EC was agreed following negotiations. This Directive requires each Member State to put in place for traditional herbal medicines a registration scheme that is, in effect, a simplified version of the normal arrangements for a marketing authorisation. Under Directive 2001/83/EC, industrially produced medicines placed on the market in the EU are required to have a marketing authorisation based on demonstration of safety, quality and efficacy. Following Directive 2004/24/EC, for traditional use registration, the normal quality standards for medicines will apply; however, the requirement to demonstrate efficacy is replaced by evidence of traditional use; also, unless there are particular concerns, the safety requirements will in most cases be met by reference to bibliographic evidence, rather than by a requirement for tests and trials.

- 7.4 The UK background is that some herbal medicines have a marketing authorisation. However, most manufactured herbal remedies have hitherto been sold as unlicensed medicines under the longstanding provisions of Section 12(2) of the Medicines Act 1968, which subject to certain conditions, exempts herbal medicines from the requirement for a licence. This existing UK scheme has few safeguards for the public as regards safety and quality of the product or accompanying product information and is widely regarded as inadequate to meet current expectations.
- 7.5 There is persistent evidence of low grade unlicensed herbal remedies on the UK market posing a risk to public health. Problems include adulteration of remedies with heavy metals or pharmaceutical ingredients, contamination, erroneous inclusion of toxic herbs, and labelling which fails to give the consumer accurate information about the safe use of the product. The MHRA (and its predecessor the Medicines Control Agency) has had on a number of occasions issued alerts to public about such remedies. Further information about these safety issues is available on *Herbal Safety News*, the MHRA's website publication available at www.mhra.gov.uk.
- 7.6 The Directive is significant in public policy terms in that, hitherto, much of the UK herbal medicine sector has been largely unregulated whereas in future it will be required to come within the systematic regime of medicine regulation, albeit with the regime tailored to reflect the particular characteristics of herbal medicines.
- 7.7 During the negotiations on the Directive, and after its agreement, the MHRA has carried out extensive consultation and dialogue with interested parties. In addition to formal consultations the MHRA has held regular meetings with the industry's Herbal Forum (representing all known UK manufacturers' trade associations operating in this field) as well as over 40 meetings with individual companies. In response to the most recent consultation on transposition 60 responses were received from the herbal sector (eg industry and practitioner representatives) and from other interested parties. The RIA (see section on Consultation) reports the outcome of the consultation, and a more detailed report on consultation is on the MHRA's website.
- 7.8 There has been wide recognition in the UK herbal sector of the need for the Directive, though there have been a range of specific concerns expressed. During the negotiations on the Directive the main concerns expressed by some in the UK herbal sector about the scope of the scheme were accommodated through amendments to the draft proposals. The amendments achieved greater flexibility to take account of evidence of traditional use of herbal remedies outside the European Union; and the ability to permit the inclusion of ancillary added vitamins and minerals to traditional herbal remedies.
- 7.9 The main area of current concern within parts of the UK herbal sector in relation to the Directive concerns specific aspects of the quality requirements, as set out in European quality guidelines for herbal medicines. The quality guidelines have a legislative base in the Directive; however the detailed guidelines are drawn up by European scientific and regulatory committees based as the European Medicines Agency (EMA). There are some anxieties in parts of the UK herbal

sector as to whether elements of the herbal quality guidelines, as they apply to those traditional herbal medicines containing a large number of ingredients, are realistically achievable, particularly by smaller companies. These updated European guidelines have been the subject of a recent consultation by the EMEA and the outcome is awaited.

- 7.10 In recognition of the feedback during consultation that parts of the herbal UK industry will need a significant period of time to adapt to the new requirements the Directive is being implemented in the UK to utilise in full the transitional period permitted under the Directive (until April 2011) for products that were legally on the UK market at April 2004.
- 7.11 An independent expert advisory committee is being established under the Herbal Medicines Advisory Committee Order 2005 to advise Ministers and the MHRA in relation to the operation of the traditional herbal medicine registration scheme established under Directive 2004/24/EC. In addition the committee will consider representations made where the Licensing Authority is minded to take an adverse decision, for example refusal of an application for traditional use registration.

8. Impact

- 8.1 A Regulatory Impact Assessment is attached to this memorandum.
- 8.2 The impact on the public sector primarily relates to the MHRA. The MHRA is the competent authority responsible for granting product registrations in accordance with the Directive 2004/24/EC. The MHRA will charge fees for the work carried out in accordance with the Directive. The fees are charged directly to companies who seek and receive the service being provided. There is no cross- subsidisation involved. The level of fees will be monitored to ensure they are set at the right level and proposals will be made to adjust them at a later date if not.

9. Contact

- 9.1 Alison Daykin at the Medicines and Healthcare products Regulatory Agency (tel: 020 7084 2404; or e mail: alisondaykin@mhra.gsi.gov.uk) can answer queries regarding the instrument.

**FULL REGULATORY IMPACT ASSESSMENT: DIRECTIVE ON
TRADITIONAL HERBAL MEDICINAL PRODUCTS (DIRECTIVE 2004/24/EC)**

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REGULATORY IMPACT ASSESSMENT: THE DIRECTIVE ON TRADITIONAL HERBAL MEDICINAL PRODUCTS

1. This RIA relates to the transposition and implementation of Directive 2004/24/EC amending Directive 2001/83/EC as regards traditional herbal medicinal products.

PURPOSE AND INTENDED EFFECT OF THE PROPOSAL

Objective

2. The Directive aims to:
 - protect public health while applying the principles of proportionality
 - provide a harmonised legislative framework for the regulation of traditional herbal medicinal products
 - contribute to the free movement of relevant goods in the single market.

Introduction

3. The Directive introduces for manufactured traditional herbal medicinal products that are suitable for use without medical supervision a modified version of the existing European licensing scheme for regulating industrially produced medicinal products. The Directive requires standards to be met relating to the product: safety, quality, patient information; also standards relating to manufacture, wholesale and import. The Directive requires each Member State to set up a registration scheme by October 2005. The key feature of the Directive is that instead of the normal requirement for those wishing to place a medicine on the market to demonstrate efficacy of the product, under this scheme evidence of traditional usage will be required. The scheme is not, however, available where the regulatory authority judges that the product satisfies the requirements, including in relation to efficacy, for a marketing authorisation.
4. The proposal therefore affects principally those involved in the manufacture, distribution, and sale of herbal remedies that are covered by this Directive. In order to register a product an applicant has to submit a detailed dossier including expert reports. Those wishing to manufacture or wholesale require licences will be subject to inspection by the MHRA.
5. Directive 2004/24/EC amends Directive 2001/83/EC. A separate Directive, 2004/27/EC, is simultaneously amending Directive 2001/83/EC to reflect the outcome of the 2001 Review of the European regulatory framework for medicines. A number of provisions of that Directive make amendments that will have an impact on the traditional herbal medicines registration scheme required to be implemented under Directive 2004/24/EC. For convenience, the more significant new requirements of Directive 2001/83/EC as amended by Directive 2004/27/EC as they impact on traditional herbal medicines are also flagged up in this RIA. Except where indicated to the contrary all further references to “the Directive” and to costs refer to Directive 2004/24/EC.

Background

The regulation of herbal medicines in the UK and EU

6. Medicinal products are regulated under specific European and domestic legislation. The primary piece of European legislation is Directive 2001/83/EC (as amended, most recently by Directive 2004/27/EC), of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use. Hitherto the European legislation has made no distinction between medicines made from herbal or non herbal ingredients, although there have for some years been a number of European guidelines which are specific to herbal medicines. Some non specific legislation also applies to medicinal products. For example, Directive 85/374/EEC on product liability provides protection for the consumer. This Directive is implemented by the Consumer Protection Act 1987 and applies in part to medicinal products.
7. Currently, herbal medicines intended for general retail sale reach the UK market by two different routes:
 - a marketing authorisation can be obtained from the licensing authority under the Medicines for Human Use (Marketing Authorisation Use) Regulations 1994 (SI 3144/1994) which largely transposed Directive 2001/83/EC into UK law. Under the Regulations most industrially produced medicinal products that are placed on the market are required to be authorised. Authorisation is obtained by demonstrating standards of quality, safety and efficacy.
 - Section 12(2) of the Medicines Act 1968 (and regulation 1(3) of the 1994 Regulations) exempts herbal remedies that are not required to have a marketing authorisation from the requirement for a product licence (required under the Medicines Act), providing the remedy meets various conditions. Certain ingredients are prohibited or restricted, but otherwise there are no specific requirements as to safety, quality or efficacy. No written claims are permitted for these remedies and there is no specific requirement to give the consumer systematic information about the safe usage of the product.
8. Although several hundred herbal medicines have a UK marketing authorisation, most herbal remedies on general sale reach the market place by using the exemption provided for in Section 12(2) of the Medicines Act.
9. In other EU Member States the route of obtaining a marketing authorisation under Directive 2001/83/EC has also been available, although in practice it is used much more widely in some Member States than others. A study for the European Commission, which preceded this legislative initiative, showed that there was a variety of pragmatic arrangements that in practice served to allow herbal medicines to be on national markets either within or outside this regulatory framework. As a consequence, the regulatory impact on industry of Directive 2004/24/EC is likely to vary between Member States. It is likely to be larger in the UK where much of the industry has been operating in a substantially unregulated environment.
10. It was long acknowledged that various of these national arrangements lacked a secure legal basis and that this complex pattern of arrangements hindered the free movement of goods. There were particular problems with the UK regime which has been widely perceived within the UK herbal sector itself, and by other interested parties, as failing adequately to protect public health.

Rationale for Government intervention

11. There are clear public health risks associated with the UK arrangements for unlicensed herbal remedies. Evidence of these risks has continued to accumulate since the Directive was agreed and in September 2004 the MHRA updated an earlier warning

about the erratic safety and quality of some traditional Chinese medicines (TCMs) on the market. Some of the problems have been on a significant scale with products containing harmful ingredients actually or potentially distributed to a considerable number of outlets and patients. For example, in December 2004 the MHRA confiscated a consignment of 90,000 tablets reportedly containing a toxic ingredient, and in 2003 the MHRA found that a product containing 11.7% mercury by weight was available in 35 traditional Chinese medicine outlets.

12. The World Health Organisation is encouraging the international trend towards more systematic regulation of herbal medicines in the interests of public health.

Risks to public health

13. There is an extensive international trade in unlicensed herbal remedies and there has been evidence in the UK, and internationally, of low grade unlicensed herbal remedies that are prone to problems of:
 - accidental or deliberate substitution of herbal ingredients with alternative, sometimes toxic, herbal ingredients
 - contamination or adulteration, e.g. with undeclared prescription only pharmaceutical ingredients or heavy metals
 - mislabelling.
14. Product surveys and enforcement activities have identified these problems both in UK and elsewhere. These problems often stem from poor manufacturing standards in parts of the sector. Testing of raw herbal drugs and products labelled as containing Fang Ji or Mu Tong on the UK market showed over 40% of samples tested to contain aristolochic acids, thus confirming widespread substitution with *Aristolochia* species. In 2000 the Agency investigated 75 sites that were thought to be supplying skin lightening creams illegally containing pharmaceutical ingredients in the form of cortico steroids. The Agency found that 62 outlets were indeed contravening the Medicines Act. (*Report by the Comptroller and Auditor General - January 2003*)
15. Cases periodically come to light where the public has actually been harmed, with a requirement for hospital treatment for serious conditions such as kidney or liver failure. However, it is likely that only a small proportion of the total cases of actual harm caused by low grade herbal medicines are identified as busy clinicians will typically have no reason to know or suspect that an undeclared ingredient is the cause of a health problem and survey evidence shows that the public often don't tell their doctor that they are taking herbal remedies. Even where products may otherwise be of good quality, there may be a lack of adequate and reliable safety information about the use of the product, for example whether it is safe to use in pregnancy or by children or whether there are known contra-indications. Given the nature of the problem neither regulators nor academics have been able to produce overall estimates of the incidence of harm. However, there is consistent evidence of the persistence of products on the market that present a clear, and in some cases immediate and serious, risk to public health.
16. Herbal medicines, like any other medicines, can lead to adverse reactions or can interact with other medicines. The risk therefore arises particularly where unlicensed products are not labelled to give the consumer systematic information about the safe use of the product. The issue of interactions is documented in scientific literature. An example of the issue of interactions is St John's Wort. The table below also illustrates that there is under reporting of adverse incidents in relation to herbal medicines:

Timetable	Number of UK yellow card (adverse reaction) reports relating to SJW	Number of reports which specifically included herb/drug interactions
Oct 1996 – Feb 2000	35	7
Since Feb 2000 (<i>when issue of SJW interactions made public</i>)	108	34

17. The all party House of Lords Science and Technology Committee was very clear on the need for improved regulation of herbal remedies.

“We are concerned about the safety implications of an unregulated herbal sector and we urge that all legislative avenues be explored to ensure better control of this unregulated sector in the interests of the public health.”¹

Risks to responsible businesses

18. In the absence of set quality standards, those manufacturing to good quality standards have complained to MHRA that they are undercut on price by those who buy low grade ingredients inadequately tested and controlled, for example as to identity and purity.
19. Where a licensed product has to comply with label warnings, e.g. on pregnancy, lactation; unlicensed herbal remedies do not. This is likely to have the effect that the consumer may believe that the unlicensed product (often without systematic warning information) is safer and that the product is suitable for wider use (e.g. in pregnancy).

Risks to public confidence

20. The public has no reliable means of knowing which unlicensed herbal remedies are made to adequate standards and which are not.
21. Surveys of unlicensed herbal products have illustrated that a proportion of products may fail to contain stated amount of ingredients (e.g. inclusion of excess waste material or use of parts of plant not believed to be efficacious).

OPTIONS

22. There are three principal options: :

- **Option 1:** Maintain the status quo, ie fail to implement Directive 2004/24/EC.
- **Option 2:** Implement a statutory registration scheme for traditional herbal medicines as required by the Directive but without taking full advantage of any areas of flexibility within the Directive and without taking a proactive approach to helping industry adjust to the new arrangements. Under this approach the UK might set a shorter transitional period than permitted under the Directive, for example to end by 2006. The principle effect of this “minimalist” approach to implementation would be

¹ (House of Lords Science and Technology Committee Inquiry into Complementary and Alternative Medicine (Nov 2000))

that companies would have only a limited time in which to ensure that products on the market at April 2004 complied with the Directive.

- **Option 3:** Implement a statutory registration scheme for traditional herbal medicines as required by the Directive while seeking to give UK industry maximum opportunity to adjust successfully to the new requirements. This would entail allowing products legally on the market at April 2004 to remain on the market until the latest date permitted (April 2011) before they are required to be registered and comply with the Directive. The MHRA would also take a range of practical measures to help industry to prepare for the Directive, including holding individual company meetings, running workshops and providing early website guidance on the Directive.
23. It is proposed on the basis of the following considerations that under either option 2 or 3 the registration scheme would be run by the MHRA, in line with its normal role in regulating medicines:
- the desirability of a consistent approach, based on expert scientific knowledge and regulatory experience, to public health issues relating to the safety of medicines - irrespective of whether medicines are made of herbal, non herbal ingredients or a combination
 - the desirability of a consistent approach to the full range of other regulatory issues relating to OTC medicines including quality standards, consumer information, assessment, inspection, enforcement
 - the Agency's extensive expertise and experience in operating regulatory arrangements for licensed herbal remedies and for homoeopathic medicines
 - the fact that there will continue to be a wide range of herbal medicines with a marketing authorisation, unlicensed herbal remedies supplied under S12(1) by herbalists, as well as those with registrations under the proposed scheme; there is a need for a consistent regulatory approach. It is likely that in some cases for a given herbal remedy there may be some products with a marketing authorisation and others with a traditional use registration, depending on the indication.

Comparison of the benefits and burdens

Option 1

24. Failure to implement the Directive would be a clear breach of the UK obligations to comply with Community law and as such would be likely to lead to early infraction proceedings by the European Commission. It would not protect public health. It would send out an international signal that the UK was a haven for those wishing to manufacture and supply herbal medicines in an unregulated environment. It would perpetuate all the existing weaknesses of the present arrangements as well as leaving industry in a very uncertain position. This option is not regarded as realistic and is not considered further.

Option 2

25. This option would meet the UK's obligation in European law. However, if the MHRA only allowed a short transitional period for products on the market at April 2004, this would be likely to cause parts of UK industry substantial difficulty. A number of UK businesses are small or micro and/or have only limited experience of medicines regulation. Potentially this option could lead to companies going out of business, significant loss of consumer choice and considerable turbulence in the short to medium term. In principal this option could bring in improved public health protection more quickly than would be the case with Option 3, however, the sharp reduction in choice likely to occur over a short period could lead to greater use of unregulated products for example purchased over the internet. Thus, while better than Option 1 on public health grounds, the benefits of Option 2 would not necessarily exceed those of Option 3.

Option 3

26. This option would meet the UK's obligation in European law and would also progressively protect public health and boost public confidence. It would also maintain consumer choice. There would, however, be a longer period, ie until 2011, during which unlicensed manufactured medicines, potentially made to variable standards, could continue legally to be marketed. This option gives small business the best opportunity of adapting to the new requirements and of making what in some cases may need to be significant acquisition of expertise and upgrading of standards, potentially including substantial adaptation to, or move of, premises.
27. The remainder of the RIA focuses on Option 3 as likely to deliver the desired benefits while giving the UK herbal sector reasonable opportunity to adjust to the new arrangements.

COSTS AND BENEFITS

Business sectors affected

Size of the UK market

28. As highlighted in the House of Lords Select Committee's report on complementary and alternative medicine, comprehensive information on the use of herbal medicines in the UK is lacking. There are a number of estimates available but it is difficult to gauge usage accurately as many products could be classified as a food rather than a medicine for regulatory purposes and the public in many cases would be unlikely to know which herbal products were classified as medicines. However, a nationally representative random telephone survey of 1204 British adults, commissioned by the BBC in 1999, suggested that around 7% of those contacted had used herbal medicines in the last year. Another survey contacted over 5000 randomly selected adults in England (not the United Kingdom) by post. Around 20% of the respondents had bought an over-the-counter (OTC) herbal remedy in the last 12 months.
29. One report (Key Note Market Assessment) estimated the market in herbal medicines was somewhat over £70 million in 2000, while another (Mintel) estimated the retail value of the market at around £65million in 2000. A more recent Mintel report (March 2003) estimated the herbal medicine sector (excluding traditional Chinese and Ayurvedic medicines) had grown to £75m in 2002 and a 2005 Mintel report again noted there was continuing growth in the market. Nicholas Hall's Insight magazine estimated the retail value of herbals in relation to the 12 months to September 2002 as around £105m. Again, all these estimates must be regarded as broad brush, given that some companies may not always have a clear and accurate view as to which of their products would be classified as medicines.
30. Future growth in the industry remains vulnerable to adverse publicity arising from issues over the safety and quality of remedies.

Structure of market

31. Analysis of the market structure for unlicensed herbal medicines is complicated by a number of factors:
 - many herbal products are borderline as to whether they should be classified as medicines or fall within other regulatory categories (foods, cosmetics or general consumer products)

- under the current regulatory regime there is no requirement for companies to submit products to the Agency for determination of whether they are medicinal products or not
 - a number of companies supply herbal ingredients (e.g. for use for herbalists or by manufacturers) rather than manufacture S12(2) products themselves.
32. The Herbal Forum, representing UK manufacturers' trade associations operating in the herbal sector, has indicated to the MHRA that it is difficult to make fully reliable estimates of the number of UK companies presently involved in manufacture of S12(2) herbal remedies.
33. The best estimate of MHRA is that there are several dozen UK manufacturers of unlicensed herbal remedies placed on the market under S12(2) of the Medicines Act 1968. A proportion of these also manufacture licensed herbal medicines. Most of the companies in this sector are either micro (having fewer than 10 employees), small (less than 50 employees) or medium (less than 250 employees) sized. Some come from a longstanding background of manufacturing herbal remedies while others may have moved in from another sector such as health foods. In addition, a very wide range of herbal remedies for the UK market is manufactured by companies in other countries including the USA, China, India, Switzerland and elsewhere in the EU.
34. The MHRA has invited any companies wishing to register products under the Directive to notify the Agency of its provisional plans and information gained in this way has helped to inform the above estimate.
35. The size of a company's product range of unlicensed herbal products which might be classified as medicines varies widely from a handful to several hundred. Typically, where a manufacturer has a range of several hundred catalogue items there will be a significant proportion of these which – depending on their presentation - would not be classified as medicines; or would be used by herbalists as ingredients; or which may be classified as medicines but which are intended for herbalists' use only and whose composition is driven primarily by herbalists' professional requirements.
36. A wide range of retailers are involved in the sale of traditional herbal remedies. These include major chains of supermarkets, pharmacists, and health food retailers as well as a wide range of independent pharmacists and health food retailers. The National Association of Health Stores estimated that there are around 1,300 independent health food stores in the UK. There is also a significant trade in direct mail and internet sales. Some herbal practitioners also have branched out into sale of OTC herbal remedies.

Benefits of Option 3

37. The following benefits are expected:-
- ◆ **improved public health protection** through appropriate safety and quality controls and the provision of systematic authorised information; in particular:
 - fewer people unwittingly taking herbal remedies which could be dangerous or unsuitable for their needs
 - more people able, safely, to take herbal remedies suited to their needs on the basis of informed choice
 - more effective dissemination of information in the event of safety concerns arising with a particular remedy; more effective identification of the need for product recall and more effective product recall.
 - ◆ **increased consumer confidence leading to increased sales, to the benefit of consumer and business.** This would be a likely consequence of:

- the introduction of a scheme for traditional herbal medicines giving them greater recognition and status; in particular the launch of the scheme could provide a major marketing opportunity to promote the benefits of assured quality
 - as compared with the current Section 12(2) regime, products will be allowed to carry written indications for use which should help to increase consumer understanding and facilitate more effective promotion of products by business
 - the improved clarity of message which can be given by business, health professionals, regulators and other interested parties in advising the public, when seeking an OTC herbal remedy made to assured standards, to use licensed or registered products.
- ◆ **a range of other benefits to business:**
- **improved ability to plan for the future** resulting from the creation of a legally secure regulatory home
 - **some reduction for business in the difficulties in trading in herbal remedies across the EU.** The extent of the reduction in practice remains to be seen and will for example depend partly on the effectiveness of the European Herbal Medicinal Products Committee
 - **a more level playing field between companies** operating in different parts of the herbal medicines sector, arising in particular from the introduction of set quality and manufacturing standards
 - much **greater transparency in the regulatory framework** than is currently the case with the Section 12(2) regime. It is difficult to give clear, systematic guidance on a number of issues relating to the current regime
 - in some cases the item generating the cost identified is also likely to be accompanied by some **financial savings or increased value to products.** Compliance with Good Manufacturing Practice supported by advice given by Agency inspectors, for example on quality systems, can result in a range of benefits: less reworking or reprocessing needed, reduced wastage, improved stock control, lower inventory holding costs, fewer complaints, improved productivity, and decreased equipment downtime. In discussions with the Agency some individual manufacturers have also indicated that they would see the acquisition of a Manufacturer's Licence as an indicator of quality and as potentially financially beneficial to them.
- ◆ **some financial savings to the health service** resulting from fewer people requiring treatment as a result of taking adulterated or toxic remedies or a poorly labelled one unsuited to their needs.
38. In most cases it is not possible to quantify estimates for these benefits. The likely cost savings to the NHS are not insignificant. For example there have been sporadic cases where the need for organ transplant and dialysis has been linked to herbal remedies containing undeclared ingredients, and other cases of hospitalisation including use of intensive care facilities. Such known cases in aggregate may cost many tens of thousands of pounds. It is not realistically possible to estimate the potentially significantly larger numbers, types and costs of NHS treatments that are likely to arise where the causation - patients taking unsafe, low grade herbal remedies, that are poorly labelled or are adulterated – remains undetected.
39. The benefits for public health would also be tangible in situations where it is necessary to update patient information to reflect new safety information. Under the Directive this could be achieved via systematic variations to product registrations for a known range of products. This reliable method is not available with the current unlicensed regime.

Costs of option 3 for businesses, charities and voluntary organisations

40. This proposal should not significantly affect charities or voluntary organisations.
41. The businesses most directly affected by the Directive would be those involved in the manufacturer, sale and supply of finished OTC herbal medicines. Costing information is given in tables below in relation to registration of products, manufacture, wholesale (including import).
42. There would be no direct compliance costs falling on retailers other than ensuring that any herbal medicines they sold were ones with an appropriate marketing authorisation or traditional use registration.
43. The person holding a product registration will in some, but not necessarily all, cases also be the manufacturer.
44. Following discussions with a number of individual companies, the MHRA has concluded that the clearest way of presenting costing information relating to the Directive is to identify the main areas of cost relating to the Directive and to give estimates or ranges of those costs. This is accompanied by explanation of why some of the costs are likely to vary considerably between companies depending on their individual circumstances. Discussions with individual companies have underlined the fact that because existing standards vary widely many of the possible additional costs of the Directive will also vary accordingly.

Costs to individual companies

45. Costing information is set out in the tables below. Broad conclusions that can be drawn from the work on costing are that:
 - the additional costs associated with registering a product under the Directive as compared with the cost a company currently incurs in placing it on the largely unregulated market as an unlicensed herbal remedy could typically run into a figure of several tens of thousands of pounds – but the figure will vary widely, depending on many different factors relating to the nature of the product and the circumstances of the individual company
 - costs faced by companies relating to registration will not necessarily be closely correlated to the size of the company. Factors that may be more relevant include the type of products for which registration is sought, and the extent to which the company has existing quality controls in place, Size may be relevant, for example, micro and small companies may be less well equipped to carry out certain activities in-house and may need to buy in help. On the other hand, a medium sized or larger company that wishes to enter a number of European markets may well decide it is worth having state of the art dossiers and quality controls in order to minimise the risk of delay arising from queries from the various regulatory authorities
 - of the overall costs the MHRA's fees are in many cases likely to represent a relatively small proportion; of greater overall significance will be the cost of demonstrating that the product meets the requirements of the Directive. The fees are more significant in certain cases, notably where an applicant proposes ingredients that have not previously been assessed
 - products that are multi-ingredient present particular technical challenges in quality control. It will be relatively demanding to demonstrate that such products comply with the requirements of the Directive
 - with subsequent registrations of relatively similar products some costs are likely to reduce per registration, eg a greater proportion of work on preparing dossiers may be

carried out in-house using existing resources rather than by consultants once companies have acquired successful experience

- companies are likely to explore ways to manufacture more economically. For example, with relatively low selling herbal medicines the overall cost of regulation could be much less onerous where one company manufactures for several others using “own label” arrangements. Likewise companies may well organise batch production more efficiently than is often the case at present in the unlicensed sector to contain the impact of batch testing requirements
- the costs associated with regulation represent a recognition of the fact that manufacturing any OTC medicine is a significant undertaking requiring considerable knowledge, expertise and company infrastructure
- the additional costs are likely to be offset by higher sales to the extent that the public are attracted by the concept of complementary medicine made to assured standards of safety and quality; and to the extent there is media interest, advertising and publicity linked to the early years of the scheme.

Overall costs to industry

46. Given the numerous variables it is not realistic to make predictions about the overall cost of the regulation for the herbal sector as a whole. This will be heavily dependent on the behaviour of individual companies and the collective effect of individual decisions about which products to place on the market. It is clear from MHRA’s discussions with companies that many are still at the relatively early stages of determining their business strategy in relation to the Directive. But, for illustrative purposes, if by 2011 around 500 products had been registered incurring various costs relating to registration at an average of £40,000 per registration, and if about 50% of the registrations related to UK companies, this would represent a cost to UK companies of about £10m spread over 6 years for bringing these products into regulation.
47. The above figure does not include some additional expenditure, notably in premises or equipment improvement, that some companies have recognised were needed in the interests of good standards irrespective of the Directive but may have been holding back on while they developed their overall business strategy in response to the Directive.
48. There is a wide range of measures which various parties are taking or could take which have the effect of containing costs. These include:
 - the European Pharmacopoeia’s ongoing programme of work to create herbal monographs. These avoid the need for the applicant to identify and validate standards. The British Pharmacopoeia is also working on monographs in the ethnic medicines sector
 - scientific or other parties may be able to supply dossiers that will assist the European Herbal Medicinal Products Committee in the preparation of positive list and monographs. This will depend on how the Committee chooses to organise this area of its work
 - trade associations or other parties could create master files of evidence relating to traditional use, safety and patient information
 - the use of quality master files for herbal active ingredients would reduce overall costs.

Costs associated with registering a product under Directive 2004/24/EC

<i>Cost and type (policy or implementation)</i>	<i>Cost</i>	<i>Comment</i>
Product registration fees (I)	£500 - £3375 per product (higher in a minority of cases)	<ul style="list-style-type: none"> • Range covers majority of typical relatively simple products • Higher figures £6k+ would apply to certain products that are more complex to assess, eg requiring more in-depth safety assessment
Preparing dossier (I)	£within existing resources - £10k x several for each product; but could be higher in some cases	<ul style="list-style-type: none"> • Costs will vary widely, for example: are preparations carried out largely in-house within existing resources or require extensive external input eg from consultancy; does product comply with the European positive list in which case no work on safety or traditional use is required; do documents need translation; is data on quality available in orderly form; is safety problematic, requiring significant amounts of research and extensive input from safety expert before signing off safety report • Some companies may follow mixed approach, eg buying consultancy help for one or a few product(s) and then preparing most elements of future dossiers themselves
Demonstrating quality control of ingredient(s) and finished product, including stability testing (P)	Below £10k to £50k plus per product	<ul style="list-style-type: none"> • A lower figure may apply where company already has good quality controls in place and needs to make only limited adjustment, eg strengthening its existing procedures for stability testing. • The additional costs will be higher where a company has only limited existing controls in place and in particular is wishing to register a product that presents more complex quality control problems, for example multi ingredients products • Figure may be increased if a company goes for “state of the art” quality, for example if the priority is not cost minimisation but to be able to enter many EU markets while minimising risk of delay resulting from query by regulators
Staff training (I)	Nil – several £k	<ul style="list-style-type: none"> • Position likely to vary between companies as to whether training is accommodated within normal patterns of training or substantial additional input required. The figure could be significantly higher if a company has little expertise in herbal medicines.
Submission of advertising material to industry’s pre-vetting arrangements (I)		<ul style="list-style-type: none"> • This is not a compulsory cost and is not inherently linked to the Directive.
<i>User testing of patient information (2004/27/EC) (P)</i>		<ul style="list-style-type: none"> • Guidelines to be published.
<i>Product information in Braille (2004/27/EC) (P)</i>	<i>c10% increase in overall cost of the product</i>	<ul style="list-style-type: none"> • <i>Partial RIA on Directive 2004/27/EC included estimate for marketing authorisation holders of an additional 5% - 10% increase in overall costs, but suggested figure may be higher in some cases</i>

Costs associated with manufacturing a product under Directive 2004/24/EC

<i>Cost and type (policy or implementation)</i>	<i>Cost</i>	<i>Comment</i>
Capital costs of improvements to premises or equipment (P)	£0 - substantial	<ul style="list-style-type: none"> • Some companies will already comply with GMP as they have Manufacturers Licence • MHRA informal visits suggest that companies with deficient premises typically are aware of shortcomings and intended to make improvements irrespective of the Directive • Some companies may wish or need to purchase HPLC equipment, or stability testing cabinets.
Quality systems in manufacture (P)	Cost neutral	<ul style="list-style-type: none"> • On basis of MHRA informal visits assume that if manufacturer does not already have quality systems in place, cost of putting in place likely to be offset by savings, eg from reduced wastage, improved stock control etc
Employing/contracting a Qualified Person for GMP (P)	Nil –£10k x several	<ul style="list-style-type: none"> • Many companies will already have a QP, or someone who will meet the transitional requirements; costing assumes a part time appointment
Inspection (I)	£1300	<ul style="list-style-type: none"> • A daily fee is proposed. Figure shown based on inspection taking one full day.
Manufacturers's Licence (I)	Nil - £2444	<ul style="list-style-type: none"> • Some companies will already hold a Manufacturer's licence
Staff training (I)	Nil – several £k	<ul style="list-style-type: none"> • Position likely to vary between companies as to whether training is accommodated within normal patterns of training or substantial additional input required

Costs (including ongoing) associated with wholesale dealing under Directive 2004/24/EC

<i>Cost and type (policy or implementation)</i>	<i>Cost</i>	<i>Comment</i>
Employing/contracting a Responsible Person (P)	Nil in many cases	<ul style="list-style-type: none"> The RP is responsible for ensuring that the conditions of the WL are met and that the guidelines on Good Distribution Practice (GDP) are complied with. Many wholesaleddealers are likely already to have staff who could fulfil this role
Inspection (I)	£1100 or £600	<ul style="list-style-type: none"> Lower figure represent half day inspection
Wholesaleddealers licence	£1402 or £600	<ul style="list-style-type: none"> Depending on turnover
Retesting products on import (P)	Variable	<ul style="list-style-type: none"> Cost only applicable to wholesaleddealers who import Imported batches will require testing in the UK or elsewhere in the EU in accordance with the requirements of the regulatory dossier, unless there is a Mutual Recognition Agreement in place with the exporting country (Australia, New Zealand, Canada and Switzerland).
Staff training (I)	Nil – several £k	<ul style="list-style-type: none"> Position likely to vary between companies as to whether training is accommodated within normal patterns of training or additional input required

Ongoing costs associated with having products registered under Directive 2004/24/EC

<i>Cost and type (policy or implementation)</i>	<i>Cost</i>	<i>Comment</i>
Periodic fees for each registered product (P)	£75	<ul style="list-style-type: none"> Annual figure
Variations to product registration (I)	£142 - £224	<ul style="list-style-type: none"> Typical fees for a variation; higher fees payable in certain situations
Pharmacovigilance inspection (I)	Nil - £1300+	<ul style="list-style-type: none"> Separate pharmacovigilance inspection only where a problem has been identified; then daily fee rate would apply
Pharmacovigilance – access to medical advice (P)	Occasional	<ul style="list-style-type: none"> Costs can be contained by collective action (eg by trade associations)
Pharmacovigilance – regular scanning of databases (P)	Unclear at this stage	<ul style="list-style-type: none"> Costs can be contained by collective active (eg organised by trade associations) to avoid duplication. One company has estimated £10k as an overall annual cost for the various ongoing pharmacovigilance requirements.
6 monthly Periodic Safety Update Reports (PSURs) following product registration (2004/27/EC) (P)	Unclear	<ul style="list-style-type: none"> In principal, PSURs are less burdensome than preparing renewal dossiers However, UK raising in Europe whether the initial 6 monthly frequency of PSURs is necessary in all cases for traditional herbal medicines
Electronic adverse drug reaction reporting (2004/27/EC) (P)	Various – see comments	<ul style="list-style-type: none"> Standard off shelf IT package for small company c25K. MHRA is to offer alternative service to convert ADRs into required format for a fee.....

Ongoing costs associated with manufacturing products registered under Directive 2004/24/EC

<i>Cost and type (policy or implementation)</i>	<i>Cost</i>	<i>Comment</i>
Ongoing batch testing and quality controls	Varies widely	<ul style="list-style-type: none"> Will be different for every company, depending on number and type of products and what controls the company currently operates.
Regular inspection of Manufacturing site (I)	£1300+	<ul style="list-style-type: none"> Daily fee; incurred by holder of the manufacturers licence approx every 2 years (3 years abroad), unless there is need for additional “for cause” inspection
Variations to Manufacturers Licence (I)	£100 - £400	
Manufacturers Licence annual fee (I)	£307	
Ensuring Active Pharmaceutical Ingredients comply with GMP (2004/27/EC)(P)	Unclear	<ul style="list-style-type: none"> Many suppliers of APIs likely to be at or near GMP standards already, bearing in mind extensive range of herbal medicines in EU with a MA. Could lead to some increase in price of ingredients in certain parts of the sector where standards are lower

The Agency's fees

49. The Agency operates as a trading fund. There is a requirement that fees must be set at a level to cover the costs of assessment work carried out by the Agency. In line with its normal practice, the Agency has proposed a differentiated fee structure to reflect the fact that the Agency's costs are likely to vary depending on the type of product.
50. The issue has been raised as to whether it would be feasible to charge lower fees for small business, or lower fees in relation to products made on a small scale. Under Treasury guidelines, fees should reflect the work required to be carried out by the Agency. Thus differential fees can be justified in relation to certain cases, e.g. some kinds of inspection where the size of the business is relevant to the amount of work required. However, there is no current basis for assuming that the Agency's costs would be lower in relation to applications for registration submitted by small business. There is no legal basis for requiring one kind of business to cross subsidise another; and neither would it be a justified use of taxpayer's money to subsidise the registration fees of some businesses.

EQUITY AND FAIRNESS

51. This section considers how equity and fairness would be affected by Option 3, and in particular in comparison with the current regulatory position.
52. Vulnerable members of society should progressively be better protected. The requirement for systematic provision of information to the consumer under this Option should enable safer, more informed use of the product and in particular should better protect those with serious illness from the exaggerated claims sometimes made for unlicensed herbal remedies.
53. There are a number of issues of equity reflecting the varying position of companies:
 - companies which currently meet high standards of quality and safety, (either because they have licensed products or because they voluntarily meet such standards while operating under S12(2)), can currently be undercut on price by manufacturers who do not meet such high standards. Likewise the reputation and sales of responsible companies can also be undermined by the activities of the less responsible, as adverse publicity may reflect on the sector as a whole. Option 3 should address this problem by requiring consistent standards, thereby achieving a more level playing field. A number of companies – including those from both herbal medicines and health food backgrounds – have told Ministers or the Agency that they do not believe that all their competitors are manufacturing to high standards
 - some companies are concerned that others take advantage of the weakness of Section 12(2) to put products on the market of apparently indeterminate legal status (as to the regulatory category of the product). Option 3 should bring greater transparency and encourage business to make clear decisions about which regulatory regime they are seeking to follow
 - companies which invest significant resources, including conducting clinical trials, to demonstrate clinical efficacy of medicines in order to get a marketing authorisation may be concerned that in future, under Option 3, other companies

will be able to give indications for use giving the impression that efficacy is demonstrated without having to provide scientific evidence of efficacy. Product information will make clear that the usage is based on tradition

- companies making relatively early applications under the Directive may be concerned that their products, bearing the costs of systematic regulation, may be undercut and lose out in the market to largely unregulated products, potentially operating to lower standards, during the transitional period. If companies are concerned that this situation may apply to them they can defer some or all of their applications for existing products until the latter part of the transitional period.
54. As regards race equality issues, the Directive sets standards that apply to traditional herbal remedies in the EU from whatever tradition. In practice, use of remedies from some traditions, eg traditional Chinese medicines, is not at all restricted to particular ethnic communities in the UK. A significant proportion of those involved in the manufacture and supply of medicines from some ethnic traditions are likely to come from the ethnic background concerned.
 55. There have been concerns expressed that the Directive does not fully recognise some traditions, for example, it does not extend simplified registration of products to traditional medicines containing animal parts, which have considerable use in traditional Chinese medicine; or that it does not aim to provide a regulatory regime for a whole medicine system such as Ayurveda. In this respect the aim of the Directive is intentionally more limited – to provide suitable regulation, particularly as regards safety, quality, and patient information, for OTC herbal medicinal products from whatever tradition they are drawn. There is no policy intention to provide a separate regulatory system for all medicinal products within any particular system of traditional medicine. For medicines not covered by the Directive it remains open, as it was previously, for an applicant to seek a marketing authorisation for any medicine, herbal or otherwise, from any tradition. This would be based on demonstration of safety, quality and efficacy.
 56. The MHRA recognises that in some non western traditions of medicines that use herbal remedies there is considerable emphasis on remedies made up by or commissioned by practitioners. These remedies are not the subject of this Directive. Different legislation covers such remedies and there is a separate programme of reform under consideration within the UK.
 57. The overall impact of the Directive on minority ethnic groups *relative* to other communities is difficult to assess at this stage. Potentially it is likely to be significantly lower for any ethnic traditions, such as traditional Chinese medicine and Ayurveda, where a relatively high proportion of remedies is made up by a practitioner or is commissioned by practitioners to meet the needs of individual patients. On the other hand there are factors that would counteract this, position. Where OTC products from these traditions do require registration, the current evidence of patchy quality standards, notably in traditional Chinese medicine, suggests that the impact of having to meet systematic quality and manufacturing standards could be relatively higher. Also, multi ingredient products prevalent in some ethnic medicine traditions are technically more challenging in terms of overall quality control and are subject to somewhat higher registration fees on account of the greater assessment time required.
 58. The MHRA notes that the Chinese and Indian Governments have in various ways been looking to modernise and upgrade manufacturing standards for traditional medicines, for example by improving compliance with Good Manufacturing

Practice standards. If these efforts are successful they may lead to an increased proportion of traditional medicines from non western traditions able to meet regulatory standards in the UK and elsewhere in the EU.

59. The Directive should have no substantial impact on rural issues. However, to the extent that the Directive increases public confidence in and demand for herbal medicines this could be beneficial to herb growers in the UK, particularly those that can demonstrate to buyers that they grow in good conditions.

SMALL FIRMS IMPACT TEST

60. It is clear that a substantial proportion of UK businesses affected by the Directive consists of micro, small or medium sized enterprises.
61. The Agency has had very extensive dialogue with a wide range of trade associations representing different sectors of business and many of these, such as the Small Growers and Producers Association, have micro/small businesses among their membership. The Herbal Forum, with which the Agency has had extensive dialogue, has a substantial proportion of micro/small businesses among its membership. Among the initiatives undertaken have been (pre-agreement on the Directive) a programme of visits to individual business including micro/small businesses and (post-agreement on the Directive) individual company meetings at the Agency to give companies advice on their initial plans to register products.
62. The Agency also sought the advice of the Small Business Service (SBS) and the Better Regulation Task Force (BRTF) as to whether there were any further areas that could be explored in terms of helping industry to adjust to the new regulatory requirements. There were no additional suggestions other than that reported at para 75.
63. Overall, a very extensive programme of activities, also including workshops and training events has been designed by the Agency with the needs of small business in mind. Likewise the MHRA understands from parts of industry that operates pan Europe that it was one of the first Agencies in the EU to issue initial advice and informal guidance on preparing for the Directive. The MHRA has taken this approach not least in order to be helpful to business that is small and/or inexperienced in regulatory matters.
64. Nonetheless, the MHRA recognises that manufacturing medicines, herbal or otherwise, and placing them on the market is a serious undertaking which on public health grounds requires a significant infrastructure, for example in terms of suitable premises and equipment, detailed technical knowledge, trained staff, and quality systems. It is clear that the requirements of the Directive will place considerable demands on some companies that may hitherto have lacked substantial elements of such an infrastructure. This may particularly be the case where such companies are engaged in the manufacture of those herbal medicines that present particular challenges in terms of quality control, such as multi- ingredient products.

COMPETITION ASSESSMENT

65. The proposed Directive will impact primarily on manufacturers, wholesalers and retailers of herbal medicines, but will also potentially have implications for businesses involved in the markets for other herbal and natural health products or health products generally. An assessment is set out in **Annex A**.

ENFORCEMENT AND SANCTIONS

66. Apart from its weaknesses in relation to public health, the current UK regulatory regime for unlicensed herbal medicines has a number of drawbacks in terms of lack of legal clarity. It should be possible to achieve greatly improved clarity of regulatory regime under Option 3. This in turn should bring advantages for both the regulator and the regulated in terms of transparency in relation to enforcement.
67. The new regulatory arrangements would be enforced by the Agency's Enforcement Group as part of its existing compliance and enforcement responsibilities in protecting public health. Breaches of regulations will be subject to investigations and, where appropriate, cases may be liable for prosecution. Such investigations will be instigated reactively as the result of referrals to the Agency or as a pro-active response following identification of a risk.
68. The Agency will continue to build on its existing website guidance about the Directive alongside existing and any supplementary European guidelines.
69. There will be further liaison as necessary with local government enforcement authorities. Guidance will explain the rights of companies to make representations against proposed decisions on licensing/registration.

MONITORING AND REVIEW

70. Under the Directive the European Commission is required to review the scope of the Directive three years from its entry into force. This date was set to allow sufficient time for the effectiveness of the Directive to be gauged. This will in particular provide an opportunity to assess whether the scope of simplified registration might be extended to other categories of traditional medicines.
71. The MHRA is seeking regular feedback on the implementation programme, for example via feedback from workshop participants. The MHRA regularly seeks feedback from the industry's Herbal Forum on priorities in relation to implementation. The MHRA will have also continue to have regular dialogue with industry in order to identify any areas where European guidelines on herbal medicines could usefully be introduced or modified to reflect practical experience of the scheme.

CONSULTATION

Nature of consultation and dialogue

72. Discussions within Government have been principally with other parts of the Department of Health, the Food Standards Agency, the Cabinet Office and the Small Business Service. The devolved administrations have also been kept informed of the main developments on the Directive.
73. The advice of the Better Regulation Task Force was sought.
74. There has been a very extensive programme of written consultation and face to face dialogue with some dozens of external organisations and interested parties. This has taken a wide range of forms:

- a formal public consultation in the spring of 2002. This was extended by one month until the end of July in order to allow those with concerns to provide more specific evidence; an informal consultation on transposition was held in 2004, with a further formal consultation on transposition held in 2005
- Agency meetings with interested parties in the herbal sector, for example in advance of key negotiating meetings in Europe
- meetings between Ministers and interested parties
- regular MHRA meetings with the Herbal Forum, The Forum represents all UK manufacturers trade associations known to be operating in the herbal medicines sector as well as the umbrella group representing herbal practitioner organisations. Membership of the Forum consists of:
 - The Health Food Manufacturers' Association
 - The Proprietary Association of Great Britain
 - The British Herbal Medicine Association
 - The Council for Responsible Nutrition
 - The Natural Medicines Manufacturers' Association
 - The Health Food Institute
 - The Ayurvedic Trade Association
 - The Trade Association of Producers and Suppliers of Ayurvedic Products from India
 - The Chinese Medicine Association of Suppliers
 - The European Herbal Practitioners Association
 - The College of Practitioners of Phytotherapy
 - The Aromatherapy Trade Council
 - The Small Growers and Producers Association
- the MHRA has run or arranged workshops and training events, and has participated in a range of external workshops, conferences and seminars
- visits to individual companies and a programme of dozens of meetings with individual companies

75. Following the Directive taking formal effect the main focus of discussions on implementation has been with the Herbal Forum.

Overall response to consultation and dialogue

76. A wide range of organisations and individuals have been appreciative of the extent and nature of consultation and discussion that took place in the run up to the Directive. Subsequently the MHRA has received considerable positive feedback about the extent of help given to companies seeking to adjust to the new requirements.

77. Overall, the dialogue with interested parties before and during the negotiations greatly helped the Agency identify UK priorities for the negotiations. The key UK objectives thus identified were achieved in negotiations, notably an extension to the scope of the Directive to permit ancillary vitamins and minerals to be added to herbal remedies, and greater flexibility to take account of evidence of traditional use from outside the EU. The clear majority of interested parties from within and outside the herbal sector at meetings and in other ways expressed views that were at least broadly supportive of the Directive and in a number of cases strongly so. Common themes of this support were: the need to give the public greater protection and

assurance as to the quality and safety standards of the medicines they were taking, including the provision of reliable information: and the need to establish a level playing field, removing the previous adverse incentives for responsible businesses that followed high standards. A minority, predominately from within the health food sector, were either opposed or at least had very strong reservations, regarding the proposals as over-regulatory in various aspects as to the scope of the Directive and its technical requirements.

78. Following the Directive taking formal effect, the dialogue between the Agency and the Herbal Forum has focussed in particular on three main areas:

- identifying areas relating to implementation on which industry would welcome guidance or other forms of help; and planning to deliver that help or to facilitate other parties to do so
- exploring the Herbal Forum's concern about the interpretation of the provision in the Directive that applicants should be required to apply for a full marketing authorisation rather than a traditional use registration where the product satisfies the requirements of the former. The Forum has been concerned that if this provision is applied widely the costs and regulatory burden of applying for a full marketing authorisation may not be realistic for many companies. The MHRA has stated that in its experience and best understanding of the law only a relatively limited number of herbal medicines satisfy the requirements for a full marketing authorisation
- the Herbal Forum has sought advice on the possibility of modification and/or pragmatic application of some of the technical standards in the European guidelines. The MHRA has indicated that where there is flexibility explicit or implicit within the guidelines the MHRA will consider carefully case by case where an applicant makes the case that a particular element of a guideline is not applicable or is not feasible for technical reasons. A particular example is the legislative requirement that applicants should supply the qualitative and quantitative particulars of all the constituents of the product. The European guidelines on herbal medicines indicate that, for the finished product specification, where constituents with therapeutic activity are not known (which will sometimes be the case with herbal ingredients) markers may be used instead. The Agency advised the Forum that if it is looking for further helpful elaboration of these guidelines, for example in relation to the finished product specification of multi ingredient products, it would be helpful for UK industry to discuss with their counterparts in Europe and collectively put a reasoned case to the European Herbal Medicinal Products Committee.

79. In the most recent consultation, the main responses, as regards regulatory impact were:

- there was strong support within the sector for the proposal to make full use of the permissible transition period (ie until 2011) to give industry time to adapt; a minority of respondents, from outside the sector, expressed the view that the length was overly generous in view of the case for protecting public health
- there was emphasis on the significant numbers of SMEs which manufactured multi-ingredient products along with concern that costs of registering such products, and in particular in demonstrating compliance with quality requirements and meeting registration fees, would have a detrimental effect on parts of the sector. (The RIA has been adjusted to reflect this emphasis in the responses)
- concerns were expressed as to whether elements of the existing European guidelines on the quality of herbal medicines were realistic and achievable, particularly for SMEs and in relation to multi-ingredient products. The case was argued for adjusting some of the existing European quality guidelines relating to herbal medicines. The

industry's Herbal Forum reported their intention to submit comments to the European Herbal Medicinal Products Committee

- a number of respondents felt that the figure of £40,000 was conservative as a possible indicative figure for the cost of bringing a product to registration
- some respondents considered that with the requirements of the Directive it would not be financially viable for herbal practitioners themselves to engage in small scale manufacture of OTC herbal remedies
- concern about the position in areas of the sector, including ethnic medicines such as TCM, where remedies were made up by or for practitioners to meet the needs of individual patients. (In fact the Directive is not intended to cover remedies made up by or for practitioners to meet individual needs, which is the subject of separate legislation. A separate programme of regulatory reform currently under consideration in relation to practitioner remedies would determine regulatory impact on this activity)
- greater flexibility was sought on the question of who is able to sign the expert report on safety that accompanies applications to register products. (The MHRA intends to respond positively on this issue)
- overall, a number of respondents from within the sector predicted, (particularly if European quality guidelines were not adjusted) there would be, variously, substantial rises in the price of products, loss of consumer choice and loss of employment
- the Royal College of GPs felt that the savings to the health service from the Directive were understated. (The MHRA agrees this may well be the case, however, the Agency is not aware of anyone having developed a methodology for quantifying the costs to the health service arising from inappropriate use of unlicensed remedies, not least those erratically containing undeclared and toxic ingredients).

80. In relation to the Better Regulation Task Force the main area for discussion was over transitional arrangements on which the MHRA agreed with the Task Force's assessment that, on balance, it would be better not to have a cut off date by which companies would be required to notify the Agency if they wished to benefit from the transitional protection for existing products.

Identifying any other costs

81. There will be substantial compliance costs for the Agency. Hitherto the Agency has a number of functions in relation to unlicensed herbal remedies - such as provision of advice to companies, enforcement of the law and provision of advice to health professional and the public in the event of adverse incidents relating to unlicensed remedies. In general, however, there has been no requirement for the Agency to have detailed regulatory involvement with most unlicensed herbal remedies. There are significant costs involved in setting up and then running a new regulatory scheme for traditional herbal medicines. The MHRA's fee levels are set on the basis of recovering those costs. The fee levels have been the subject of a separate consultation.

SUMMARY AND RECOMMENDATIONS

OPTION	COSTS	BENEFITS	RISKS
1	None	No perceived benefit in terms of protecting public health. Will maintain consumer choice and no additional regulatory burdens will be placed on businesses	Continuing weakness in public health protection. A positive decision to go down this route likely to <i>increase</i> risk to public health by encouraging international businesses looking to target unregulated markets. Adverse incentives for business looking to operate to high standards. Decline in public confidence likely. Would hinder UK companies from increased trade with other Member States. Self – regulation would prove difficult and probably ineffective due to strong adverse incentives for responsible companies. Continuing lack of transparency in regulation. Continuing legal instability and uncertainty; strong risk of challenge; and high risk of infraction proceedings.
2.	Significant cost of introducing systematic regulatory regime into hitherto largely unregulated sector of the medicines market. Reliable cost estimates not possible as this depends on company strategies currently being formulated. But on one illustrative assumption the cost to UK companies of bringing products into regulation might be around £10m spread over several years.	Enhanced public health protection; more informed consumer choice; improved public confidence.	Significant loss of consumer choice in short to medium term if UK companies are given insufficient time to adjust to introduction of systematic regulation. This could jeopardise some of the increased public health protection. Some companies likely to go out of business. Choice likely to grow again in medium term onwards as other companies move to fill gaps in market place. Some rationalisation in area of multi-ingredient products.
3	Significant cost of introducing systematic regulatory regime into hitherto largely unregulated sector of the medicines market. Reliable cost estimates not possible as this depends on company strategies currently being formulated. But on one illustrative assumptions the cost to UK companies of bringing products into regulation might be around £10m spread over 2005 - 2011.	Enhanced public health protection; more informed consumer choice; improved public confidence; continuing wide consumer choice as companies are given substantial transitional period to adjust to the new requirements.	Some rationalisation in market, eg fewer brands likely to be available in relation to herbal remedies for which there is low demand. Some rationalisation in area of multi-ingredient products.

COMPETITION ASSESSMENT

1. Introduction

- The Directive will impact primarily on manufacturers, wholesalers and retailers of herbal medicines, but will also potentially have implications for businesses involved in the markets for other herbal and natural health products or health products generally. The market is complex and many herbal products are borderline for classification as medicines or in other regulatory categories such as food, cosmetics or general consumer products. On the demand side, herbal medicines compete, variously, with other forms of complementary and alternative medicine, other natural health products and with conventional medicines. On the supply side there is a degree of substitutability reflecting the likelihood that there may be numerous broadly comparable remedies intended for similar indications.
- The Directive will also impact upstream in the supply chain, notably on companies who supply ingredients to manufacturers. Regulatory requirements relating to the quality of the product fall on the manufacturer, however the Directive will affect the quality requirements manufacturers in turn place on suppliers of ingredients.
- The requirements for testing of products and ingredients will also affect the market in the provision of this service.
- The market relating to remedies made up by professional herbalists for individual patients in the light of face to face consultation, although not covered by this Directive, may be affected in a more indirect way. Herbalists may stand to benefit from the improved overall confidence in herbal medicines likely to follow from the Directive; they may also be able to benefit by making use of the more secure, well documented supply chain likely to result from the Directive where the herbalists purchase ingredients for their herbal remedies.
- Herbal medicines account for the greatest share of the complementary medicines sector accounting for over half the value of sales in the complementary medicines market (Source: Mintel; Complementary Medicines, March 2005). There are at least several dozen UK manufacturers of unlicensed herbal medicines placed on the market under Section 12(2) of the Medicines Act 1968. A working assumption, based on the dialogue MHRA has had with several dozen individual companies, is that there may be around 50. The Herbal Forum, representing UK industry manufacturing trade associations, has not been able to provide a more definite figure. This reflects the complexity of the market in this area. A proportion of these companies also manufacture licensed herbal medicines. The UK companies in the herbal medicines sector are generally micro, small or medium sized; a number have fewer than 10 employees. A number of companies supply herbal ingredients (e.g. for use by herbalists or by manufacturers) rather than manufacture Section 12(2) products themselves. In addition, a wide range of herbal medicines are manufactured by companies in other countries including USA, China, India, Switzerland and elsewhere in the EU.
- The Agency believes that, overall, there is not likely to be a significant concentration in the market shares of businesses involved in the manufacture of herbal medicine, although there may be issues in very specific parts of the sector. Several dozen

companies are in discussion with the MHRA about the possibility of registering products, although in the event it is possible that not all may do so, and in particular in the first year or two of operation of the Directive

- A wide range of retailers are involved in the sale of traditional herbal medicines. These include major chains of supermarkets, pharmacists and health food retailers as well as a wide range of independent pharmacists and food retailers. The National Association of Health Stores has estimated that there are around 1,300 independent health food stores in the UK. There is also likely to be a significant trade in direct mail and Internet sales. A number of practitioners appear also to have branched out into sales of OTC herbal remedies.

2. The current level of competition in the Herbal Traditional Medicines market

- The Agency understands that there is significant competition in most and possibly all parts of the market and through most or all parts of the supply chain, including supply of ingredients, manufacture, wholesale and retail. However, there is not a level playing field and competition is significantly distorted by lack of agreed underpinning quality and manufacturing standards and by imperfect information for consumers, retailers and other parties who are not in a position to know which products are made to acceptable standards. An example of how imperfect information can distort competition in the current market is that a responsible manufacturer of herbal remedies may take care to include detailed product information about safe usage of a herbal medicine, whereas a less well scrupulous producer of a broadly similar product may not research and then include the various safety, warnings and contraindications. It is likely that some consumers will erroneously assume that the latter product is the safer.
- The MHRA believes, and has also been told this by many operators in the sector, that the regulatory regime hitherto has not represented a level playing field.
- Currently, there are no specific requirements for a manufacturer of unlicensed herbal medicines to have any expertise in herbal medicines, knowledge of quality control, trained staff, or suitable premises and equipment. The Directive will introduce the consistent standards needed in these areas to protect public health and to give the consumer assurance.
- The current weak UK regulatory regime presents few barriers to entry. However, anecdotally, the Agency is aware that some companies, e.g. from elsewhere in the EU, are deterred by the fact that it is not possible to make written medicinal claims for unlicensed remedies. They would prefer to operate with a regime where the consumer can be given information about the stated purpose of the products and where there are agreed standards.

3. The Competition Filter

- The Agency has applied the Cabinet Office's "competition filter" to determine whether a simple or more detailed competition assessment is required. Against the criteria the MHRA has decided that a simple assessment is required on the basis that: the market in manufacturing of herbal medicines is not dominated by a single or few players; the regulation would not lead to higher set up or ongoing costs for new or potential firms that existing firms do not have to meet; and the sector is not characterised by rapid technological change.

4. The impact of the proposals on competition

- The introduction of systematic regulation into a hitherto largely unregulated area is likely to have a significant impact on the operation of the market.

Entry into the market

- The barriers to entry to the market for manufacturers will in future be considerably higher than hitherto, since in future entry will depend on a company having established a suitable infrastructure (premises, equipment, personnel and systems) for making herbal medicinal products to assured standards. Similar requirements will apply to existing players by the end of the transitional period.
- Over time there are likely to be some new entrants to the UK market from elsewhere in EU encouraged by the steps the Directive represents towards gradual harmonisation of the market. (Similarly there are likely over time to be greater opportunities for UK companies in the EU). The speed of harmonisation in the market will not necessarily be rapid, and will for example partly depend on the speed at which the European positive list of substances is developed by the European Herbal Medicinal Products Committee. It is likely that there will be some new companies/new products entering the UK market that had hitherto been deterred by the weakness of the UK regulatory regime for unlicensed herbal medicines.
- The Directive permits the inclusion of vitamins and minerals in traditional herbal remedies. Previously such products would have been required to meet the more onerous regulatory provisions for a full marketing authorisation. Over time this provision may have the effect of further encouraging manufacturing companies from a health food background to enter or expand into the herbal remedies sector. However, the likelihood of this remains unclear and will depend significantly on regulatory developments elsewhere, for example in relation to health claims for food, which may influence the relative attractiveness and feasibility of different regulatory routes to the market.
- Most OTC essential oils products are currently not sold as medicines and there is no reason for this situation to change. However, it is possible that one or more manufacturers might consider seeking registration for products, for example in order to test the commercial benefits of making minor medicinal claims.
- One of the regulatory costs of the Directive is testing of products and ingredients to ensure quality and safety standards. The Agency's visits to the UK herbal sector suggest that there is already a competitive market in testing herbal products and ingredients, with some companies testing ingredients and products themselves and others contracting out the work. As an additional option, companies could also consider having testing carried out elsewhere in the EU. It is possible that the new requirements may promote further entry into the market.

Existing companies

- Those existing manufacturers that operate to low standards and have little or no technical knowledge and expertise required to manufacture herbal medicines to assured standards may struggle to adjust to the new arrangements. Some may acquire such expertise during the transitional period and go on successfully to compete; however, it is likely that others may withdraw from the market. It is likely that if

there are manufacturers for whom herbal remedies are not a major component of the business such operators may decide either to withdraw from the market or to build up their capacity.

- The Directive allows a transitional period before existing products have to meet the new requirements. This will assist in reducing the scale of any impact for businesses affected by the proposal by enabling them to spread their costs. Examples include the costs of registering products and of stability testing. This allows existing operators some temporary advantage over new entrants who would be required to meet all the requirements of the Directive from the outset. This may have the effect of reducing market entry during the transitional period. It is likely that some companies will decide to test the market during the transitional period by seeking a small number of registrations in the first instance to assess both the costs and benefits to the company of getting traditional use registrations.
- Where any operators are required to undertake significant capital works, e.g. to ensure their premises are suitable for the manufacture of medicines, there will be an opportunity cost in that the capital will not be available for alternative purposes. (However, the Agency's understanding is that, typically, where changes to premises would be required, these are ones that the company has already recognised as necessary, irrespective of the Directive).
- It is likely that manufacturers will seek to contain the overall testing costs associated with the manufacture of the product by purchasing ingredients of assured quality from those suppliers who provide certificates of analysis. There is a clear financial incentive for the provision of certificates of analysis at an early stage in the supply chain, rather than for more extensive testing later in the supply chain.

Companies from outside the EU

- The impact of the Directive on manufacturers beyond the EU is likely to vary widely. Where companies market to a number of different EU Member States, the move towards greater harmonisation may assist such companies, particularly where they already manufacture to standards at or close to the required level. The Directive will pose a challenge to those overseas manufacturers currently operating with low standards.
- The MHRA has had cause to issue repeated warnings about the erratic quality and safety standards of some unlicensed TCMs that circulate on the international markets. It seems unlikely that manufacturers responsible for such products will wish, or be able, to meet the new requirements and some may seek to continue to operate in the UK on the black market, posing a challenge to enforcement authorities. There are prospects, however, that some operators in the market will be able to comply with the requirements. To ensure fair competition for such operators, as well as protect public health, it will also be important that in any reforms of the UK regulatory scheme for unlicensed herbal medicines made up by, or for, herbal practitioners rigorous standards are applied.

Market structure

- It is likely that the Directive will provide a stimulus to various forms of co-operation. In some cases there may be mergers or takeovers in order to pool expertise and strengthen the market base, for example where companies are wishing to compete

across European markets. In other cases there may be a growth in own label manufacture arrangements, for example in situations where it may not make economic sense for a number of manufacturers all to make a particular remedy for which there is low demand. Companies who have invested in relatively expensive facilities, eg for conducting stability testing in controlled conditions, may look to use any surplus capacity to generate income.

- Quality control of remedies made using sophisticated processes, or with multiple ingredients, or with added vitamins, can present technical challenges in the control of manufacture. There is feedback that multi-ingredient products in particular are typically manufactured by SMEs.

Maximising fair competition

- In order to contain regulatory impact and to maximise competition the Agency has taken a very active approach to the provision of advice and guidance for industry through a variety of different means. This work is described elsewhere in the RIA. Early informal feedback from several companies or consultants is that the MHRA's approach may be effective in maintaining competition in that more applications for registration from companies elsewhere in Europe are likely to be forthcoming at an early stage in the scheme than would otherwise have been the case.
- The Directive will create a more level playing field than currently available between licensed and unlicensed herbal remedies.

5. Conclusion

- The Agency's view is that there is, and will continue to be, a significant level of competition in most and perhaps all sectors of the market and in all parts of the supply chain. Fair competition is currently hindered by the nature of the current regime. The requirements of the Directive will be significant for many companies and substantial for those that do not currently have suitable premises, equipment, staff, technical knowledge and systems to manufacture herbal medicines to assured quality standards. The market place may be particularly challenging for those SMEs which focus on manufacture of multi-ingredient OTC herbal remedies, since the costs associated with the quality control of such products and demonstrating compliance with quality guidelines is higher.
- There should continue to be a very wide range of herbal remedies on the market. There may well be some rationalisation within the UK market as regards both businesses and products.

DECLARATION BY THE MINISTER

I have read the regulatory impact assessment and I am satisfied that the benefits justify the costs

Signed

Date

Norman Warner, Minister of State, Department of Health

Contact point:

Richard Woodfield
MHRA
Market Towers
1 Nine Elms Lane
London SW8 5NQ

Tel: 020 7084 2068

E mail: richard.woodfield@mhra.gsi.gov.uk