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27 March 2002

Dear Sir/Madam

CONSULTATION LETTER: MLX 283

EUROPEAN COMMISSION'S PROPOSALS FOR A DIRECTIVE ON TRADITIONAL HERBAL MEDICINAL PRODUCTS

Summary

1. This letter seeks your comments on:

- the European Commission's proposals for a Directive on traditional herbal medicinal products. The Directive is in the form of an amendment to the recently codified Directive 2001/83/EC which regulates the safety, quality and efficacy of medicinal products for human use
- a partial Regulatory Impact Assessment, prepared by the Medicines Control Agency, relating to these proposals.

2. Please send replies to arrive at MCA no later than **21 June 2002**, using the pro forma attached, to:

Alison Daykin
16 – 132 Market Towers
1 Nine Elms Lane
London SW8 5NQ

tel: 0207 273 0404
fax: 0207 273 0387
email: alison.daykin@mca.gov.uk

Background

3. Development work on a possible Directive on traditional herbal medicines has taken place in Europe over several years. The MCA has held a number of discussions with UK herbal interest groups during this period and has contributed to this development process. The European Commission brought forward formal proposals for a Directive in January 2002.

4. The purpose of the proposals is to establish within the Community a harmonised legislative framework for authorising the marketing of traditional herbal medicinal products, involving a simplified registration procedure. The aim is to remove the differences which create obstacles to the free movement of medicinal products in the European Union, while ensuring protection for public health.

The proposals

5. A copy of the proposed Directive is attached at Annex B. To aid understanding of the text a summary of the main points covered by the proposals is attached at Annex C. In addition, the MCA has placed on its website (www.mca.gov.uk), fuller question and answer briefing about the Directive, based on its initial assessment of the text. The codified text is available on the Commission's web site at http://pharmacos.eudra.org.

Timetable

6. The text of the proposed Directive would require Member States to take measure to comply with the Directive by 31 December 2004 (with transitional arrangements for products on the market at the time the Directive came into force). This date is however dependent on the progress of negotiations. The likely timetable for the negotiation of the Directive is not yet clear.

Publication of comments

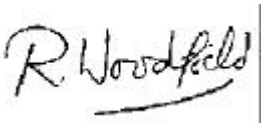
7. To help informed debate on the issues raised by this consultation exercise, and within the terms of the Code of Practice on Access to Government Information ("Open Government"), the Agency intends to make publicly available responses received to this consultation. Copies will be available shortly after the public consultation has concluded.

8. The Agency's Information Centre at Market Towers will supply additional copies of the results of the consultation on request. Copies may be further reproduced. An administrative charge, to cover the cost of photocopying and postage, may be applied. Alternatively, personal callers can inspect the replies at the Information Centre by prior appointment. To make an appointment, telephone 0207 273 0351.

9. We will assume that your comments can be made publicly available in this way unless you indicate on the pro forma at Annex E that you wish all or part of them to be treated as confidential and excluded from this arrangement. Under the Code of Practice on Access to Government Information, the Agency will not release confidential replies or replies containing personal confidential information.

10. Should you have any questions regarding the proposals or the conduct of the consultation exercise, please contact Alison Daykin (see para 2). Further paper copies of this letter and with attachments are available on request. If you consider there are other organisations that should be invited to comment on these proposals, please either pass a copy of the documents to them or contact the MCA and we will arrange for a consultation pack to be sent to them.

Yours faithfully



Richard Woodfield
Group Manager Herbal Policy

Attachments:

Annex A:	Distribution list for MLX 283
Annex B:	European Commission proposals for a Directive on Traditional Herbal Medicinal Products: ? Explanatory Memorandum ? Directive ? Impact Assessment Form
Annex C:	Summary of proposals by MCA
Annex D:	Partial Regulatory Impact Assessment by MCA
Annex E:	Pro forma for reply

Annex A

CONSULTATION LETTER MLX 283

DISTRIBUTION LIST

Advertising Association
Advertising Standards Authority
All-Party Pharmacy Group
Anthroposphical Association
Arthritis Care
Association of Anaesthetists of Great Britain and Northern Ireland
Association of British Cardiac Nurses
Association of British Dispensing Opticians
Association of British Health Care Industries
Association of British Pharmaceutical Industries
Association of Clinical Research in the Pharmaceutical Industry
Association of Community Health Councils of England & Wales
Association of Dispensing Opticians
Association of Independent Clinical Research Contractors
Association of Medical Research Charities
Association of Pharmaceutical Importers
Association of Respiratory Specialists
Association of Scottish Trusts
Association of Traditional Chinese Medicine UK
ATC
Ayurvedic Trade Association
Asthma & Allergy Research
Bioindustry Association
British Acupuncture Council
British Association of Chemical Specialities
British Association of Dermatologists
British Association of European Pharmaceutical Distributors
British Association of Homoeopathic Manufacturers
British Association of Nutritional Therapies
British Association of Pharmaceutical Physicians
British Association of Pharmaceutical Wholesalers
British Association of Research Quality Assurance
British Cardiac Patients Association
British College of Optometrists
British Complementary Medicines Association
British Contact Dermatitis Group
British Dental Association
British Dental Association (Northern Ireland)
British Dental Association (Scotland)
British Dental Association (Wales)
British Dental Trade Association
British Diabetic Association
British Epilepsy Association
British Generic Manufacturers Association
British Heart Foundation
British Herb Trade Association
British Herbal Medicines Association
British Homoeopathic Association
British Institute of Regulatory Affairs
British Medical Association
British Medical Association (Northern Ireland)
British Medical Association (Scottish Branch)
British Medical Association (Welsh Office)
British Menopause Society
British Oncological Association
British Pharmacological Society
British Retail Consortium
British Society for Allergy and Clinical Immunology
British Society for Rheumatology
British Society of Gastroenterology
British Toxicology Society
Broadcast Advertising Clearance Centre
BAAAP
CARE
Careers National Association
CCCPH
Central Medical Advisory Committee
Chemical Industries Association
Chemist & Druggist
Chinese Medical Institute & Register
Chiropodists Board
CMAS
College of Health
College of Optometrists
College of Pharmacy Practice
Common Services Agency
Commonwealth Working Group on Traditional and Complementary Health
Community Pharmacy Magazine
Community Practitioners and Health Visitors Association
Community Services Pharmacists Group
Company Chemist Association Ltd
Consolidated Communications
Consumers Association
Consumers in Europe
Consumers for Health Choice
Co-operative Pharmacy Technical Panel
Cosmetics, Toiletry & Perfumery Association Ltd
Council for Alternative and Complementary Medicine
Council for the Professions Supplementary to Medicine
Council for Responsible Nutrition
CTS Dental Supplies
Department of Health
Department of Health and Social Services (NI)
Dispensing Doctors Association
Doctor Magazine
Drug & Therapeutics Bulletin
Drug Information Pharmacists Group

English Board for Nursing, Midwifery & Health Visiting
Essential Oil Trade Association
European Association of Hospital Pharmacists
European Council for Classical Homoeopaths
European Herbal Practitioners' Association
Faculty of Family Planning
Faculty of Homoeopathy
Faculty of Pharmaceutical Medicine
Family Planning Association
Family Planning Association (Northern Ireland)
Federation of Wholesale Distributors
Food and Drink Federation
Foundation for Integrated Medicine
General Medical Council
General Medical Services Committee
General Medical Services Committee (Wales)
General Practitioners Association (NI)
Genetic Interest Group
Guild of Healthcare Pharmacists
HCSA
Health & Safety Executive
Health Development Agency
Health Education Authority
Health Food Manufacturer's Association
Health Service Commissioner
Health Which?
Help the Aged
IHRC
Imperial Cancer Research Fund
Independent Healthcare Association
Independent Television Commission
Institute of Biology
Insulin Dependent Diabetes Trust
Internal Holistic Aromatherapy Foundation
Institute for Optimum Nutrition
Institute of Quality Assurance
Institute of Health Food Retailing
International Society of Professional Aromatherapists
International Federation of Aromatherapists
Joint Royal Colleges Ambulance Service Liaison Committee
Local Authority Central Office of Trading Standards (LACOTS)
Long-Term Medical Conditions Alliance
Medical Defence Union
Medical Devices Agency
Medical Protection Society Ltd
Medical Research Council
Medical Women's Federation
Medicines Commission
MIMS (Haymarket Medical Publishing Ltd)
Ministry of Defence
National Asthma Campaign
National AIDS Trust
National Assembly for Wales
National Association of GP Co-operatives
National Association of Health Stores
National Association of Primary Care
National Association of Women Pharmacists
National Back Pain Association
National Board for Nursing, Midwifery and Health Visiting
National Board for Nursing, Midwifery & Health Visiting (NI)
National Board for Nursing, Midwifery & Health Visiting for Scotland
National Consumer Council
National Council of Women of GB
National Eczema Society
National Federation of Retail Newsagents
National Federation of Women's Institutes
National Institute of Medical Herbalists
National Meningitis Trust
National Pharmaceutical Association
Natural Medicines Manufacturers' Association UK
Natural Medicines Society
NCH & SPCS
Neonatal and Paediatric Pharmacists Group
Neurological Alliance
NHS Alliance
NHS Confederation
NHS Information Authority (Coding & Classification)
NHS Pharmaceutical Quality Control Committee
Northern Ireland Consumer Council
OTC Bulletin
OTC Business News (Informa Publishing Group Ltd)
OTC News & Market Report
Overseas Doctors Association in the UK Ltd
Paediatric Chief Pharmacists Group
Patients Association
Pharmaceutical Contractors Committee (Northern Ireland)
Pharmaceutical Journal
Pharmaceutical Quality Group
Pharmaceutical Services Negotiating Committee
Pharmaceutical Society for Northern Ireland
Prescription Medicines Code of Practice Authority
Prescription Pricing Authority
Proprietary Association of Great Britain
Radio Advertising Clearance Centre
Radio Authority
Register for Chinese Herbal Medicine
Registered Nursing Home Association
Royal College of Anaesthetists
Royal College of General Practitioners
Royal College of Midwives
Royal College of Nursing
Royal College of Nursing (Northern Ireland)
Royal College of Nursing (Scotland)
Royal College of Nursing (Wales)
Royal College of Obstetricians & Gynaecologists
Royal College of Ophthalmologists
Royal College of Paediatrics and Child Health
Royal College of Pathologists
Royal College of Physicians & Surgeons (Glasgow)

Royal College of Physicians (Edinburgh)
Royal College of Physicians (London)
Royal College of Psychiatrists
Royal College of Radiologists
Royal College of Surgeons (Edinburgh)
Royal College of Surgeons (England)
Royal College of Surgeons (Faculty of Dental Surgery)
Royal Colleges of Physicians : Faculty of Pharmaceutical Medicine
Royal Colleges of Physicians : Faculty of Public Health Medicine
Royal Pharmaceutical Society of Great Britain
Royal Pharmaceutical Society of Great Britain (Scotland)
Royal Pharmaceutical Society of Great Britain (Welsh Executive)
Royal Society of Chemistry
Royal Society for the Promotion of Health
School of Homoeopathic Medicine
Scottish Consumer Council
Scottish Executive
Scottish General Medical Services Committee
Scottish Pharmaceutical General Council
Scottish Wholesale Druggists Association
Scrip Ltd
Shadow Health Professionals Council
Social Audit
Society of Homoeopaths
Society of Pharmaceutical Medicine
Society for the Promotion of Nutritional Therapy
Sterilised Suture Manufacturers Association
Surgical Dressings Manufacturers Association
TAPASI
Terrance Higgins Trust
The British Thoracic Society
The Herb Society
The Institute for Complementary Medicine
UK Central Council for Nursing, Midwifery & Health Visiting
UK Clinical Pharmacy Association
UK Homoeopathic Medical Association
UK Inter-Professional Group
Unified Register of Herbal Practitioners
Veterinary Medicines Directorate (VMD)
Welsh Consumer Council
Women in Medicine

Annex B

COMMISSION OF THE EUROPEAN COMMUNITIES

Brussels, 17.01.2002
COM(2002) 1 final

2002/0008 (COD)

Proposal for a

DIRECTIVE OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

amending the Directive 2001/83/EC as regards traditional herbal medicinal products

(presented by the Commission)

EXPLANATORY MEMORANDUM

1. GENERAL BACKGROUND AND OBJECTIVES

The fundamental objectives of the Community's pharmaceutical legislation are to ensure the protection of public health while completing the Single Market in pharmaceuticals. To this end, Directive 2001/83/EC 1 prescribes that no medicinal product may be placed on the market without having obtained a marketing authorisation on the basis of harmonised requirements. In principle, the application for such a marketing authorisation has to contain the results of tests and trials on quality, safety and efficacy of the product. There are however some exceptions. The particulars relating to safety and efficacy need not be presented, e.g. where it is demonstrated by detailed references to published scientific literature that the product has a well-established medicinal use in the sense of Article 10(1)(a)(ii) of Directive 2001/83/EC and as defined in Part 3 of Annex I to that Directive.

This legal framework is suitable for certain herbal medicinal products. However, for many herbal medicinal products, which are being used for a long period, sufficient published scientific literature is not available so that a well-established medicinal use cannot be demonstrated. New tests and trials are in theory possible, but lead to significant financial burdens for the companies concerned, often small or medium-sized enterprises, and entail also inevitable disadvantages of such trials for animals and human beings. These consequences are difficult to justify where the traditional use of the medicinal product is of such a nature as to allow sound conclusions on its safety and efficacy. As a consequence, the legal and practical situation of traditional herbal medicinal products in the Member States varies significantly with negative impacts on the protection of public health as well as on the free movement of these goods within Europe.

The Council and the European Parliament have, on several occasions, addressed the specific situation of herbal medicinal products. In its resolutions of 20 December 1995 2 and of 23 April 1996 [3], the Council called on the Commission to study the existing situation of these products in close co-operation with the Member States. On demand of the Commission, the Association of the European Self-Medication Industry investigated the situation of herbal medicinal products in Europe and presented a report in 1998 [4]. In its resolution of 16 April 1996 [5], the European Parliament pointed to the growing demand for herbal medicinal products and the importance of this sector of pharmaceutical industry for employment opportunities especially in small and medium-sized enterprises. The European Parliament explicitly called for specific provisions on herbal medicinal products to provide optimum health protection for European citizens, to facilitate the marketing of these products in Europe as well as to ensure an appropriate involvement of experts in this field.

Against this background, the new Directive provides for a special registration procedure allowing the registration and, hence, the marketing of certain traditional herbal medicinal products without requiring particulars and documents on tests and

1. OJ L 311, 28.11.2001, p.67…
2. OJ C 350, 30.12.1995, p. 6.
3. OJ C 136, 8.5.1996, p. 4.
4. „Pflanzliche Arzneimittel in der Europäischen Union", ETD/97/501336, Abschlußbericht, November 1998.
5. OJ C 141, 13.5.1996, p. 63

trials on safety and efficacy. However, the same requirements apply to the manufacturing of these products and their quality. In order to further improve the protection of public health, the Directive provides a special legal framework for traditional herbal medicinal products, thus removing the differences and uncertainties about the status of these products currently existing in the Member States. Furthermore, the Directive harmonises the rules applicable to traditional herbal medicinal products in Europe and thereby contributes to facilitate the free movement of these goods in the Single Market.

For reasons of coherence and legibility of the regulatory framework, the specific provisions on traditional herbal medicinal products shall be introduced in the new Community code relating to medicinal products for human use, as contained in Directive 2001/83/EC. The main objective of the draft Directive is to establish a harmonised legislative framework for traditional herbal medicinal products and hence is based on Article 95 of the EC Treaty. Since the differences currently existing between the situation in the Member States constitute an obstacle to the free movement of these goods within the Community, a certain harmonisation on the European level appears necessary and is consistent with the principle of subsidiarity. The draft Directive is limited to those provisions considered indispensable to attain a sufficient degree of harmonisation while ensuring the full protection of public health and therefore respects also the principle of proportionality.

2. SPECIFIC COMMENTS

The scope of the new provisions is limited to traditional herbal medicinal products (*Article 16a*). Those herbal medicinal products, which can be authorised under chapter 1 of title III of Directive 2001/83/EC either on the basis of the results of new tests and trials on safety and efficacy or on the basis of reference to published scientific literature, shall not be eligible for the simplified registration. If either of these cases is given, especially where sufficient scientific literature is published for a given herbal medicinal product to prove its well-established medicinal use in the sense of Article 10(1)(a)(ii) of Directive 2001/83/EC, an exception from the general requirements of chapter 1 of title III of Directive 2001/83/EC is not necessary and should therefore not be allowed. With regard to particularities of homeopathic medicinal products, the new provisions shall not apply either to homeopathic medicinal products.

There are several conditions that have to be fulfilled to be eligible for the registration under the new provisions (*Article 16a*). The entirety of these conditions shall guarantee that only those herbal medicinal products have access to the simplified registration, where it is appropriate and justified to depart from the strict requirements of chapter 1 of title III of Directive 2001/83/EC. Hence, the product must be a herbal medicinal product. Furthermore, the possible indications and ways of administration are limited, while the product must be for administration with a specified strength. Finally, the period of traditional use must have elapsed and the information on the traditional use of the medicinal product must be sufficient. This condition is necessary to ensure that only traditional herbal medicinal products are granted access to the market via the registration procedure, for which the information on the traditional use allows the national authority to conclude on the safety and the efficacy of the product.

In principle, the applicant for a registration under the new provisions has to provide the same particulars and documents as for an application under chapter 1 of title III of Directive 2001/83/EC, including the results of physico-chemical, biological or

microbiological tests (*Article 16c*). Hence, relating to the quality of the medicinal product the same requirements as for an authorisation under chapter 1 of title III of Directive 2001/83/EC apply. However, instead of providing the results of tests and trials on safety and efficacy of the product, the applicant has to present bibliographical or expert evidence on the traditional medicinal use of the product as well as a bibliographic review of safety data together with an expert report. The well established medicinal use in the sense of Article 10(1)(a)(ii) of Directive 2001/83/EC, as defined in Part 3 of Annex I to that Directive, requires at least 10 years from the first systematic and documented use. Bearing in mind that a traditional medicinal use under the new provisions does not require such a systematic and documented use, a period of thirty years seems appropriate. In principle, only medicinal use within the Community is relevant since it is very difficult to verify whether information on use outside the Community provides a reliable basis to conclude on the efficacy and especially the safety of the product. However, if the product has been available within the Community for at least 15 years, it appears acceptable that the evidence of 30 years of medicinal use may fully or partly relate to such use outside the Member States.

Due to the dissimilar situation of herbal medicinal products in the Member States, which cannot immediately be harmonised in its entirety by the new provisions, the mutual recognition procedure as laid down in chapter 4 of title III of Directive 2001/83/EC cannot be applied to registrations of traditional herbal medicinal products. The new provisions oblige the Member States however to take due account of authorisations or registrations granted to the product (*Article 16d*). In interpreting this obligation, the progressing harmonisation in the field of traditional herbal medicinal products on the basis of monographs established by the new committee has to be considered.

An application for the registration of a medicinal product under the new provisions is to be refused under certain conditions (*Article 16e*). It is to be refused, if the evaluation shows that the qualitative and/or quantitative composition of the product is not as declared in the application, if the therapeutic indications do not comply with the restrictions laid down in Article 16b, if the product could be harmful in the normal conditions of use, if the data on the traditional use in insufficient or if the pharmaceutical quality is not satisfactorily demonstrated.

With the intention to further facilitate the application for certain traditional herbal medicinal products, a list of herbal substances shall be set up that fulfil the conditions of eligibility for the registration procedure (*Article 16f*). For each substance, the list shall indicate the therapeutic indication, the specified strength, the route of administration and any other relevant safety information. If an application for traditional use registration refers to a herbal substance contained in that list, the applicant, instead of supplying the respective documents, may refer to the contents of the list. Nevertheless, even in this case, the normal requirements regarding the quality of the product fully apply.

Where appropriate, the existing pharmaceutical legislation applies to the new registration procedure (*Article 16g*). This concerns:

– the exclusion of medicinal products prepared in a pharmacy in accordance with the magistral or the official formula (Article 3(1) and (2) of Directive 2001/83/EC);
– the right of Member States to apply national legislation on the sale, supply or use of medicinal products as contraceptives or abortifacients (Article 4(4) of Directive 2001/83/EC);

– the obligation that the necessary documents and particulars must be drawn up by experts (Article 12 of Directive 2001/83/EC);

– the time limit of 210 days for the decision on a valid application (Article 17(1) of Directive 2001/83/EC);

– the analysis of particulars submitted by the competent national authorities (Article 19 of Directive 2001/83/EC);

– the control of manufacturers and importers coming from third countries (Article 20 of Directive 2001/83/EC);

– the obligation of the marketing authorisation holder to take account of scientific and technical progress (Article 23 of Directive 2001/83/EC);

– the validity of a marketing authorisation for 5 years (Article 24 of Directive2001/83/EC);

– the civil and criminal liability of the manufacturer and the marketing authorisation holder (Article 25 of Directive 2001/83/EC);

– the general provisions on manufacture and importation (Articles 40 to 52 of Directive 2001/83/EC);

– the provisions on classification of medicinal products (Articles 70 to 75 of Directive 2001/83/EC);

– the provisions on wholesale distribution of medicinal products (Articles 76 to 85 of Directive 2001/83/EC);

– the provisions on pharmacovigilance (Articles 101 to 108 of Directive 2001/83/EC);

– the obligation of Member States for repeated inspections (Article 111(1) and (3) of Directive 2001/83/EC);

– the obligation to furnish proof of controls carried out (Article 112 of Directive 2001/83/EC);

– the provisions on suspension etc. of a marketing authorisation (Articles 116, 118 and 126 second indent of Directive 2001/83/EC);

– the prohibition of supply of medicinal products (Article 117 of Directive 2001/83/EC);

– certain information obligations (Articles 122 to 123 of Directive 2001/83/EC);

– certain obligations regarding administrative decisions (Article 125 of Directive 2001/83/EC);

– the certificate on manufacturing authorisation (Article 127 of Directive 2001/83/EC);

– the Directive 91/356/EEC on the principles and guidelines of good manufacturing practice.

In principle also the general provisions on labelling and package leaflet (Articles 54 to 65 of Directive 2001/83/EC) as well as on advertising (Articles 86 to 99 of Directive 2001/83/EC) apply. However, it appears necessary to ensure a full information to the public, especially the patients, about the particularities of traditional herbal medicinal products, registered under this Directive. It contains therefore, inter alia, the obligation to include in the labelling, the package leaflet and in any advertising the information that the product is a traditional herbal medicinal product and that the efficacy has not been clinically proven (*Articles 16g(2) and(3)*).

To ensure full participation and involvement of experts in the field of herbal medicinal products, a new Committee for Herbal Medicinal Products is set up within the European Agency for the Evaluation of Medicinal Products established by Council Regulation (EEC) No 2309/93 (*Article 16h*). The committee's tasks will relate to the scientific issues with regard to herbal medicinal products and herbal substances. The committee will be composed of one member nominated by each Member State with regard to their special role and experience for 3 years renewable.

One of the major tasks of the new committee will be to establish Community herbal monographs (*Article 16h(3)*). These monographs contain relevant information for herbal medicinal products, such as a definition, the constituents, clinical particulars, pharmacological properties and bibliographical references. Such monographs are relevant for the assessment of an application for a marketing authorisation based on well established medicinal use as well as of an application for registration under the new provisions. With the intention to continuously improve the harmonisation of the situation of herbal medicinal products in Europe, whenever such monographs have been adopted they must be used as basis for any application for registration under the new provisions. Furthermore, when new monographs are adopted, the registration holder is obliged to introduce a modification to the registration dossier so as to comply with the new monograph.

It is important to ensure full consistency between the Committee for Proprietary Medicinal Products and the Committee for Herbal Medicinal Products. The two committees should consult each other and, where possible, reach agreement on the position to take in case of a referral regarding an application, which relies on Article 10(1)(a)(ii) of Directive 2001/83/EC and which makes use of a Community herbal monograph. The obligation of the Executive Director of the Agency to ensure appropriate co-ordination between the scientific committees of the Agency as contained in Article 55(2) of Regulation 2309/93 should be extended to the new committee (*Article 16g(3)*). As far as legislative amendments are necessary, they will be considered during the discussions on the procedural provisions on the mutual recognition procedure.

2002/0008 (COD)
Proposal for a

DIRECTIVE OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

amending the Directive 2001/83/EC
as regards traditional herbal medicinal products

THE EUROPEAN PARLIAMENT AND THE COUNCIL OF THE EUROPEAN UNION,

Having regard to the Treaty establishing the European Community, and in particular Article 95 thereof,

Having regard to the proposal from the Commission [6],

Having regard to the opinion of the Economic and Social Committee [7],

Acting in accordance with the procedure laid down in Article 251 of the Treaty [8],

Whereas:

(1) Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use [9] requires that applications for the authorisation to place a medicinal product on the market have to be accompanied by a dossier containing particulars and documents relating in particular to the results of physico-chemical, biological or microbiological as well as pharmacological and toxicological tests and clinical trials carried out on the product and thus proving its quality, safety and efficacy.

(2) Where the applicant can demonstrate by detailed references to published scientific literature that the constituent or the constituents of the medicinal product have a well established medicinal use with recognised efficacy and an acceptable level of safety in the sense of Directive 2001/83/EC, he should not be required to provide the results of pre-clinical tests or the results of clinical trials.

(3) A significant number of medicinal products, despite their long tradition, do not fulfil the requirements of a well established medicinal use with recognised efficacy and an acceptable level of safety and are not eligible for a marketing authorisation. To maintain these products on the market, the Member States have enacted different procedures and provisions. These differences currently existing between the provisions laid down in the Member States may hinder trade in traditional medicinal products within the Community and lead to discrimination and distortion of competition between manufacturers of these products. They may also have impact on the

6 OJ ....
7 OJ ....
8 OJ C 95, 30.3.1998, p. 1.
9 OJ L 311, 28.11.2001,p.67 [As amended by Directive….(OJ,L…)]

protection of public health since the necessary guarantees of quality, safety and efficacy are not always given at present.

(4) Having regard to the particular characteristics of these medicinal products, especially their long tradition, it is desirable to provide a special, simplified registration procedure for certain traditional medicinal products. However, this simplified procedure should be eligible only where no marketing authorisation under Directive 2001/83/EC, in particular due to lack of sufficient scientific literature demonstrating a well established medicinal use with recognised efficacy and an acceptable level of safety, can be obtained. It should likewise not apply to homeopathic medicinal product eligible for a marketing authorisation or for a registration under Directive 2001/83/EC.

(5) The long tradition of the medicinal product enables to renounce clinical trials, insofar as the efficacy of the medicinal product is plausible on the basis of long-term use and experience. Pre-clinical tests do not seem necessary, where the medicinal product on the basis of the information on its traditional use proves not to be harmful in specified conditions of use. However, even the long tradition does not exclude that there may be concerns with regard to the product's safety, so that the competent authorities should be entitled to ask for all data necessary for assessing the safety. The quality aspect of the medicinal product is independent of its traditional use so that no derogation should be made with regard to the necessary physico-chemical, biological and microbiological tests.

(6) The vast majority of medicinal products with a sufficiently long and coherent tradition are based on herbal substances. It therefore seems appropriate to limit the scope of the simplified registration in a first step to traditional herbal medicinal products.

(7) The facilitated registration should be acceptable only where the herbal medicinal product may rely on a sufficiently long medicinal use in the Community. Medicinal use outside the Community should be taken into account only, if the medicinal product has been used within the Community for a certain time.

(8) With the objective to further facilitate the registration of certain traditional herbal medicinal products and to further enhance harmonisation, there should be the possibility to establish a Community list with herbal substances that fulfil certain criteria, such as being in medicinal use for a sufficiently long time, and hence do not seem harmful in the normal conditions of use.

(9) Having regard to the particularities of herbal medicinal products, a specific committee should be established within the European Agency for the Evaluation of Medicinal Products set up by Council Regulation [(EEC) No 2309/93 of 22 July 1993 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Agency for the Evaluation of Medicinal Products] [10] (hereinafter: the Agency). The committee should be composed of experts in the field of herbal medicinal products. Its tasks should relate in particular to establishing Community herbal monographs relevant for the registration as well as the authorisation of herbal medicinal products.

[10] OJ L 214, 24.8.1993, p. 1, Regulation as last amended by Commission Regulation (EC) no 649/1998 (OJ L 88, 24.3.1998, p. 7)

(10) It is important to ensure full consistency between the new committee and the committee for human medicinal products already existing at the Agency, in particular in case of a procedure regarding an application, which concerns a herbal medicinal product and relies on Directive 2001/83/EC, appropriate co-ordination between the two committees should be ensured, relying on the provisions of Article 55(2) of Regulation 2309/93.

(11) When deciding upon an application for registration of a traditional herbal medicinal product, the Member State concerned should be obliged to take due account of authorisations or registrations previously granted by another Member State for that product. In case where the authorisation or registration refers to a herbal medicinal product for which a monograph has been established under this Directive, it should be recognised, unless there are major objections of public health.

(12) The Commission should present a report on the application of the chapter on traditional herbal medicinal products to the European Parliament and to the Council including an assessment on the possible extension of traditional use registration to other categories of medicinal products.

(13) It is therefore appropriate to amend Directive 2001/83/CE accordingly,

HAVE ADOPTED THIS DIRECTIVE:

Article 1

Directive 2001/83/EC is amended as follows:

(1) In Article 1 the following points (29) to (32) are added:

«(29) Traditional herbal medicinal product:

a herbal medicinal product that fulfils the conditions laid down in Article 16a;

(30) Herbal medicinal product:

any medicinal product, containing as active ingredients one or more herbal substances or one or more herbal preparations, or one or more such herbal substances in combination with one or more such herbal preparations;

(31) Herbal substances:

all mainly whole, fragmented or cut plants, plant parts, algae, fungi, lichen in an unprocessed, usually in dried form but sometimes fresh. Certain exudates that have not been subjected to a specific treatment are also considered to be herbal substances. Herbal substances are precisely defined by the plant part used and the botanical name according to the binomial system (genus, species, variety and author);

(32) Herbal preparations:

preparations obtained by subjecting herbal substances to treatments such as extraction, distillation, expression, fractionation, purification, concentration and

fermentation. These include comminuted or powdered herbal substances, tinctures, extracts, essential oils, expressed juices and processed exudates.»

(2) The following new chapter 2a is inserted in title III.

"Chapter 2a: Specific provisions applicable to traditional herbal medicinal products

Article 16a

A simplified registration procedure (hereinafter "traditional use registration") is hereby installed for herbal medicinal products which fulfil the following criteria:

(a) they are indicated exclusively for indications adapted to a traditional herbal medicinal product, which, by virtue of its composition and purpose, is intended and designed for use without the intervention of a medical practitioner for diagnostic purposes or for prescription or monitoring of treatment;

(b) they are exclusively for administration in accordance with a specified strength;

(c) they are an oral, external and/or inhalation preparation;

(d) the period of traditional use as stipulated in Article 16c (1) (c) has elapsed;

(d) the data on the traditional use of the medicinal product is sufficient, in particular the product proves not to be harmful in the specified conditions of use and the pharmacological effects or efficacy of the medicinal product are plausible on the basis of long-term use and experience.

However, in cases where the competent authorities judge that a traditional herbal medicinal product fulfils the criteria for an authorisation in accordance with Article 6 or a registration pursuant to Article 14, the provisions of this chapter do not apply.

Article 16b

1. The applicant and registration holder shall be established in the Community.

2. In order to obtain traditional use registration, the applicant shall submit an application to the competent authority of the Member State concerned.

Article 16c

1. The application shall be accompanied by:

   (a) the particulars and documents:

      (i) referred to in Article 8(3) (a) to (h), (j) and (k),

      (ii) the results of pharmaceutical tests referred to in the first indent of Article 8(3) (i),

      (iii) the summary of product characteristics without the data specified in Article 11(4),

(iv) in case of a combination, as referred to in Article 1 (30), the information data referred to in Article 16a (e) relating to the combination as such; if the individual active ingredients are not sufficiently known, the data need also relate to the individual active ingredients;

(b) any authorisation or registration obtained by the applicant in another Member State, or in a third country, to place the medicinal product on the market, and details of any decision to refuse to grant an authorisation or registration, whether in the Community or a third country, and the reasons for such a decision;

(c) bibliographical or expert evidence to the effect that the medicinal product in question, or a corresponding medicinal product has been in medicinal use in the Community throughout a period of at least thirty years preceding the date of application;

(d) a bibliographic review of safety data together with an expert report, and where required by the competent authority, upon justified request, data necessary for assessing the safety of the medicinal product.

Annex I shall apply by analogy to the particulars and documents specified in point (a).

2. A corresponding medicinal product, as referred to in paragraph 1 (c), is characterised by having the same active ingredients, irrespective of the excipients used, the same or similar intended purpose, equivalent strength and the same or similar route of administration as the medicinal product applied for.

3. The requirement to show medicinal use throughout the period of thirty years, referred to in paragraph 1 (c), is satisfied even where the marketing of the product has not been based on a specific authorisation. It is likewise satisfied if the number or quantity of ingredients of the medicinal product has been reduced during that period.

4. If the product has been available within the Community for at least 15 years, the applicant may supply evidence of medicinal use throughout a period of time, which completes the period of 30 years in a specified territory or territories outside the Community.

Article 16d

When evaluating an application for traditional use registration, each Member State shall take due account of registrations or authorisations granted by another Member State.

Article 16e

1. Traditional use registration shall be refused if the application does not comply with Articles 16a, 16 b or 16c or if at least one of the following conditions is fulfilled:

(a) the qualitative and/or quantitative composition is not as declared,

(b) the therapeutic indications do not comply with the conditions laid down in Article 16 a,

(c) the product could be harmful in the normal conditions of use,

(d) data on traditional use is insufficient, especially if pharmacological effects or efficacy are not plausible on the basis of long-term use and experience,

(e) the pharmaceutical quality is not satisfactorily demonstrated.

2. The competent authorities of the Member States shall provide the applicant, the Commission and any competent authority requesting this, with any decision it makes to refuse traditional use registration on safety grounds and the reasons for this.

Article 16f

1. The Committee referred to in Article 16h shall set up a list of herbal substances. The list shall contain with regard to each herbal substance the therapeutic indication, the specified strength, the route of administration and any other information necessary for the safe use of the herbal substance.

2. If an application for traditional use registration relates to a herbal substance contained in the list, referred to in paragraph 1, the data specified in Article 16c (1) (b) (c) and (d) does not need to be provided. Article 16e (1) (c) and (d) shall not apply.

3. If a herbal substance ceases to be included in the list, referred to in paragraph 1, registrations pursuant to paragraph 2 for herbal medicinal products containing this substance shall be revoked unless the particulars and documents, referred to in Article 16c (1) are submitted within three months.

Article 16g

1. Articles 3 (1) and (2), 4(4), 12, 17(1), 19, 20, 23, 24, 25, 40 to 52, 70 to 85, 101 to 108, 111(1) and (3), 112, 116 to 118, 122, 123, 125, 126 second indent, 127 of this Directive as well as Commission Directive 91/356/EEC [11] shall apply, by analogy, to traditional use registration granted under this chapter.

2. In addition to the provisions laid down in Articles 54 to 65 any labelling and user package leaflet shall contain a statement to the effect that:

(a) the product is a herbal medicinal product for traditional use in a specified indication and that the efficacy of the product has not been clinically proven but relies exclusively on long-term use and experience; and

(b) the user should consult a doctor or a qualified practitioner if the symptoms persist during the use of the medicinal product.

A Member State may provide that the labelling and the user package leaflet shall also state the nature of the tradition in question.

3. In addition to the provisions laid down in Articles 86 to 99 any advertisement for a medicinal product registered under this chapter shall contain the following statement:

OJ L 193, 17.7.1991, p. 30.

"traditional herbal medicinal product for use in [specified indication] for which efficacy has not been proven".

Article 16h

1. A Committee for Herbal Medicinal Products is hereby established. That Committee shall be part of the Agency.

2. The Committee for Herbal Medicinal Products shall consist of one member nominated by each Member State for a term of 3 years, which shall be renewable. They shall, as appropriate, be chosen by reason of their role and experience in the evaluation of herbal medicinal products and shall represent their competent authorities.

3. The Committee shall establish Community herbal monographs for herbal medicinal products with regard to the application of Article [10a] [10(1)(a)(ii)] as well as traditional herbal medicinal products. The appropriate co-ordination with the committee for human medicinal products shall be ensured by the Executive Directive of the Agency according to Article 55(2) of Regulation 2309/93. The Committee shall fulfil further responsibilities conferred upon it by provisions of this chapter and other Community law.

When Community herbal monographs in the sense of this paragraph have been established they shall be used as the basis for any application.

When new Community herbal monographs are established, the registration holder shall within one year after the date of establishment of such monograph, introduce a modification to the registration dossier in order to comply with that monograph. The registration holder shall notify that modification to the competent authority of the Member State concerned.

4. The Committee shall adopt its own rules of procedure.

Article 16i

Until … [date], the Commission shall present a report to the European Parliament and the Council concerning the application of the provisions of this chapter.

The report shall include an assessment on the possible extension of traditional use registration to other categories of medicinal products."

Article 2

1. The Member States shall take the measures necessary to comply with this Directive by 31 December 2004. They shall forthwith inform the Commission thereof. When Member States adopt the said measures, they shall contain a reference to this Directive or be accompanied by such a reference when officially published.

2. For the traditional herbal medicinal products as referred to in Article 1 of this Directive, which are already on the market on the entry into force of this Directive, the competent authorities shall apply the provisions of the present Directive within five years after its entry into force.

Article 3

This Directive shall enter into force on the day of its publication in the *Official Journal of the European Communities*.

Article 4

This Directive is addressed to the Member States.

Done at Brussels,

For the European Parliament	*For the Council*
The President	*The President*

IMPACT ASSESSMENT FORM

THE IMPACT OF THE PROPOSAL ON BUSINESS WITH SPECIAL REFERENCETO SMALL AND MEDIUM-SIZED ENTERPRISES (SMEs)

TITLE OF PROPOSAL

Proposal for a Directive of the European Parliament and of the Council amending the Directive 2001/83/EC as regards traditional herbal medicinal products.

THE PROPOSAL

1. Taking account of the principle of subsidiarity, why is Community legislation necessary in this area and what are its main aims?

   The purpose of the proposed Directive is to lay down specific provisions traditional herbal medicinal products in the Community. It brings together the European experience and understanding in the field of traditional herbal medicines with the essential aim of safeguarding public health and satisfying the consumer choice. Trade in traditional herbal medicinal products within the Community is, at present, hindered by disparities between the national requirements and differences in basic traditional use concepts in EU. Specific legislation will contribute to a free circulation of these products within the Community while ensuring their quality, safety and efficacy.

THE IMPACT ON BUSINESS

2. Who will be affected by the proposal?

   – which sectors of business?

   The majority of the concerned companies belongs to the pharmaceutical sector and is manufacturing medicinal products for which the conditions of market access are modified by the present proposal. It will also have an impact on certain companies belonging either to the pharmaceutical or to the food industry since it aims at allowing the marketing as medicinal products of products which so far do not have a defined status.

   – which sizes of business? (what is the concentration of small and medium-sized firms)

   Apart from some multinational players involved in marketing herbal medicines, the vast majority of the businesses within the Community in this sector are small and medium size enterprises.

   – are there particular geographical areas of the Community where these businesses are found?

   According to different sources, France and Germany cover more than 50 % of the EU market.

3. What will business have to do to comply with the proposal (in terms of regulatory efforts)?

In the Community, there is likely to be little impact for larger pharmaceutical companies as these businesses usually manufacture all products to pharmaceutical standards and hold marketing authorisations and manufacturing authorisation. For the small and medium-sized enterprises the impact also has to be considered generally positive, even if there will be a certain impact in terms of fees and administration. The proposal's objective is not to strengthen the already existing technical-regulatory requirements. To the contrary it envisages establishing a derogatory regime in order to allow the market access of a large category of medicinal products for which certain of the existing requirements, in particular with regard to the efficacy, will not be needed any more. Those small and medium-sized enterprises which for the moment do not market these products as pharmaceuticals, will need to invest in the equipment and personnel necessary to achieve a licence for the manufacturing of medicines and to carry out the necessary quality assurance work to adequately comply with standards relating to the quality and safety of these products. Only some of these enterprises have such facilities at present. However, it needs to be taken into consideration that the conditions for marketing these herbal medicinal products will be identical in the fifteen Member States and therefore will allow an easier access to non-national markets in contrast to what is the case today.

4. What economic effects is the proposal likely to have?

– on employment

Only a limited category of companies will have to do certain investments. For these companies, the Directive's effect on the employment will certainly be positive. As mentioned above, for those companies already belonging to the pharmaceutical sector, the access to an enlarged market on the basis of harmonised conditions should increase their potential sales volumes and hence their competitiveness leading again to a positive effect on the employment.

– on investment and the creation of new businesses

For larger pharmaceutical businesses, there will probably be an increase in investment in the sector as it will increase marketability of these products. There is likely to be little impact on costs as these enterprises already manufacture all products to pharmaceutical standards.

On the other hand, certain new investments in equipment and personnel could become necessary for that category of companies marketing products, which do not possess a defined status at present. This could lead to certain activities of merger or of a transfer to other areas of business.

Overall, the effect of this Directive on the companies producing traditional medicines which is the vast majority of the concerned companies, is likely to be very positive considering the fact that the Directive offers possibilities to extend their market into other Member States and lays down new technical-regulatory conditions for this market access.

– on the competitiveness of businesses (within EU/world/wide)

Bearing in mind the heterogeneous character of the companies, it is difficult to predict the further evolution of their competitiveness as a result of adopting the Directive. However, enlarging the potential market (from national to Community), modifying the technical requirements (above mentioned derogatory regime), better information of the public and increased confidence in the security of these products should allow to improve the overall competitiveness of this sector and to outweigh the investments which will be necessary in certain companies.

5. Does the proposal contain measures to take account of the specific situation of small and medium-sized firms (reduced or different requirements etc)?

The implementation of this Directive will define standards on a European level for the group of traditional herbal medicines and will allow these products to maintain their status as medicinal products in their country of origin and to obtain it in the other Member States, permitting thus a de-partitioning of the market in this sector. Bearing in mind the increasing interest in this kind of medicinal product in the majority of the Member States, it can be expected that the overall effect on the business performance of producers of traditional herbal medicines, most of which are small and medium-sized enterprises, will be positive.

The proposed Directive will ease the burden of proof in the area of safety and efficacy, thereby reducing the requirements which apply to this kind of product at the moment.

CONSULTATION

6. List the organisations which have been consulted about the proposal and outline their main views.

The contents of the proposed Directive have been discussed intensely with the Member States and other stakeholders. Everybody supported the underlying principle of this initiative. A questionnaire on the need and possible contents of the envisaged legislation, prepared by the Commission and sent to the Member States, was discussed during the Pharmaceutical Committee in September 2000. An ad hoc working group, composed of representatives of the Commission and interested Member States, was set up and prepared a first draft. This draft was sent to the Member States for comments. At the same time, the envisaged legislation was discussed with other stakeholders. Among the various conferences where the draft Directive was addressed, especially a workshop held on the 26 January 2001 in Brussels on the review of the pharmaceutical legislation has to be mentioned. Participants to this workshop represented the major associations of patients, consumers, pharmaceutical industry, distributors, doctors, and pharmacists. On the basis of the comments received by the Member States as well as the feed back from other parties, the Commission revised the draft. This modified version was once again discussed with the Member States during the Pharmaceutical Committee in April 2001 where the Member States' representatives declared their accord. Following these discussions, the draft was a last time amended in order to take into consideration certain technical remarks.

Annex C

SUMMARY OF MAIN POINTS IN PROPOSALS FOR A DIRECTIVE ON TRADITIONAL HERBAL MEDICINAL PRODUCTS

Overview

The Directive would require Member States to introduce a simplified registration procedure. Traditional herbal medicines which could not fulfil the criteria for a marketing authorisation under the provisions of Community law relating to medicines would receive a traditional use registration, if the applicant could provide the necessary evidence of traditional use, safety and quality.

Coverage

The proposals cover medicinal products where the active ingredients are herbal. Homoeopathic medicines are not covered, neither are herbal medicines which could be given a marketing authorisation (based on demonstration of efficacy as well as safety and quality). Registrations would be restricted to herbal medicines intended for use without the intervention of a medical practitioner, whether for diagnostic purposes, prescription or monitoring of treatment. Traditional use registrations would be restricted to herbal medicines taken orally, or for external use or inhalation.

The proposals includes provision for a subsequent review of the directive with a possible later extension of traditional use registrations to other categories of medicines. (It should also be noted that any traditional medicine containing a non herbal active ingredient would not fall within the existing UK scheme under which herbal remedies may be exempt from the requirement to have a licence (as set out in the Medicines Act 1968)).

Traditional use

The applicant would need to demonstrate that the herbal medicine or "corresponding" product(s) had been in medicinal use in the European Union for 30 years at the time of the application. Evidence for up to 15 of the 30 years could relate to use outside the European Union. Corresponding products must have the same active ingredients, the same or similar intended purpose, the same or similar route of administration, and equivalent strength. The number or quantity of ingredients may have been reduced during the qualifying period of traditional use.

Applicants would need to produce bibliographic or expert evidence of traditional use. The MCA's initial assessment is that there is a very wide range of possible sources which, taken together as necessary, potentially could provide the required evidence. These include: authoritative literature on herbalism; the practical evidence of numerous licensed or unlicensed manufactured products on the market in many EU member states; the long-standing lists of herbal medicines accepted as traditional by regulatory authorities in a number of member states; and the testimony of recognised experts on

herbalism. This last source could be particularly helpful in confirming the patterns of usage of combinations of herbal ingredients.

Applicants would not need to demonstrate traditional use where the herbal substance in question was contained in the positive list of herbal substances prepared by the Committee for Herbal Medicinal Products.

Efficacy

There would be no requirement to present data on tests and trials relating to efficacy. The labelling of the product would reflect this position with the proposed wording: *"the efficacy of the product has not been clinically proven but relies exclusively on long-term use and experience"*

A registration would be refused if data on traditional use is insufficient, especially if pharmacological effects or efficacy are not plausible on the basis of long-term use and experience. The MCA expects that evidence that a herbal remedy had an accepted use within a herbal tradition over a significant period would generally represent reasonable evidence that a degree of efficacy in relation to the relevant traditional use indication was at least plausible.

Safety

The applicant would need to present a bibliographic review of safety data, together with an expert report. Regulatory authorities, where justified, would be able to ask for more data in order to assess the safety of the product. Registration would also be refused if the product is found to be harmful in normal conditions of use.

Positive list of herbal substances

There would be an agreed list of herbal substances with therapeutic indications, specified strength, route of administration and any relevant safety information. The applicant could then refer to this list rather than providing data on traditional use and safety. The applicant would still need to demonstrate quality. The positive list of herbal substances would be compiled by the proposed Committee for Herbal Medicinal Products which would be established by the Directive.

Quality

The normal quality requirements applicable to licensed medicines would apply. The MCA assessment is that the proposed quality requirements are ones which are already successfully met by companies in UK and elsewhere in Europe in relation to licensed herbal medicines. In many cases, the type of product with a traditional use registration will be very similar to a licensed herbal medicine.

Compliance with Good Manufacturing Practice (GMP) would be required of Manufacturers and Importers, and there would also be a requirement for Manufacturers, Importers and Wholesale Distributors to hold the appropriate licence (Manufacturer's Licence or Wholesale Dealers Licence).

The MCA would expect to apply the provisions of the Directive and any relevant European guidelines in a way that was appropriate to the nature of the product under consideration.

Information

Labelling and leaflets for products with a traditional use registration would include information and instructions about the safe use of the product. It would be made clear to the consumer that the indications were not clinically proven but were based on long-term use and experience. There would also be advice that the user should consult a doctor or qualified practitioner if the symptoms persisted during use of the product.

Member States would have the option of requiring that labelling and leaflets should state the nature of the herbal tradition.

The normal rules relating to the advertising of medicines would apply. In addition, any advertisement would need to contain the wording: *"traditional herbal medicinal product for use in [specified indication] for which efficacy has not been proven*".

The Committee for Herbal Medicinal Products

The Committee would be part of the European Agency for the Evaluation of Medicines and have the following main functions:

- establishing Community herbal monographs
- setting up and maintaining a positive list of herbal substances in relation to which applicants did not need to demonstrate safety and traditional use.

The Committee would consist of one member nominated by each Member State for a renewable term of three years.

Review of the Directive

By a specified date (not yet stated in the proposals) the European Commission should present to the European Parliament and the Council a report on the operation of the Directive. This should include an assessment on the possible extension of traditional use registration to other categories of traditional medicinal products.

Transitional arrangements

The Directive would come into force at the point it is published in the *Official Journal of the European Communities* (that is at around the time of successful completion of the negotiations)

By 31 December 2004 Member States would be required to have put in place a scheme complying with the Directive. (Any specific date of this kind may need to be adjusted to reflect the progress of negotiations on the Directive.)

Within five years from the Directive coming into force, Member States must have applied the provisions to products which were already on the market at the time the Directive came into force.

Annex D

PARTIAL REGULATORY IMPACT ASSESSMENT

Proposal for a Directive of the European Parliament and of the Council amending Directive 2001/83/EC as regards traditional herbal medicinal products

Purpose and intended effect of the proposal

1. The Commission's proposal aims to:

   - provide a harmonised legislative framework for the regulation of traditionally used herbal medicinal products[1]
   - contribute to the free movement of relevant goods in the single market
   - protect public health while applying the principles of proportionality.

2. The proposal applies to herbal medicines for human use. The period for demonstrating traditional use is 30 years within the European Community. (Up to 15 years of use outside the EU can be used to qualify for part of the 30 year period). The Directive covers medicines which are for minor medical indications; are suitable for use without the intervention of a medical practitioner; and which are unable to satisfy the efficacy requirements necessary for a marketing authorisation. Labelling requirement would give the consumer systematic information about the safe use of the product and make clear that the indications were based on tradition rather than proof of efficacy. The principle requirement of the scheme for companies would be demonstration of the traditional use of the medicine for specified minor indication(s), and its safety and quality.

Risk assessment

3. Current regulation of herbal medicines in the UK fails to provide an adequate balance between protecting the consumer and providing consumer choice. At present, herbal medicines intended for general retail sale can 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 transposed the relevant Community legislation relating to medicines into UK law. This requires products to meet standards of quality, safety and efficacy. This route protects public health but in practice the requirement to demonstrate efficacy tends to limit consumer choice in relation to benign herbal remedies making limited claims.

   - Section 12(2) of the Medicines Act 1968 (and regulation 1(3) of the 1994 Regulations) exempts herbal medicines from the normal requirement for medicines to have a marketing authorisation or product licence, providing the remedy meets certain conditions. Certain ingredients are prohibited or restricted, but otherwise there are no specific requirements as to safety, quality or efficacy. Consequently, this route does not adequately protect public health, although it does provide the consumer with a wide choice.

[1] A medicinal product is: a) any substance or combination of substances presented for treating or preventing disease in human beings or animals *or* b) any substance or combination of substances which may be administered to human beings or animals with a view to making a diagnosis or to restoring, correcting or modifying physiological function in human beings or animals is likewise considered as medicinal product.

4. 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.

5. Ministers, the MCA, and the Committee on the Safety of Medicines (CSM) which provides independent scientific advice, have concerns over the low quality and safety standards of some unlicensed herbal medicines on the UK market, with the problem particularly noticeable in certain ethnic herbal medicines. The toxic herbal ingredient *Aristolochia*, now banned in unlicensed medicines, has been found in traditional Chinese medicine (TCM) products, probably as a result of deliberate or accidental substitution of species. This plant contains active substances (aristolochic acids) which are carcinogenic and have been associated with kidney failure in two UK patients and the subsequent development of cancer in one of these patients. The Agency has found toxic levels of arsenic or mercury in some TCMs. On occasions, potent prescription only medicines, which can legally only be made available by a prescription from a doctor or dentist, have also been found in herbal medicines sold directly to the public by herbal practitioners. Also, the Agency remains concerned about the continuing illegal adulteration of unlicensed Chinese 'herbal' creams with prescription only steroids. The MCA held a press conference in September 2001 to alert the public, via the media, to these continuing concerns and to publicise CSM's advice that it was not currently possible to give any general assurances as to the safety of TCMs on the UK market. Since then the MCA has continued to find further examples of such problematic products. It is not readily possible for the public to identify which TCM products may have been made to higher standards.

6. The lack of systematic and mandatory product and safety information on unlicensed herbal remedies can compound public health risks. The use of preparations of St. Johns Wort (SJW) illustrates this point. The use of this herbal remedy has become increasingly popular for the self-treatment of mild depression. SJW can have a variety of effects on the central nervous system and can reduce the effectiveness of some major prescription medicines including, amongst others, oral contraceptives, antidepressants, anticonvulsants and treatments for HIV infection. The introduction of statutory product information would help minimise avoidable adverse reactions to medicines and 'herb-drug' interactions. MCA currently has to depend on voluntary co-operation from trade associations in relation to warnings on products. However, there are inherent weaknesses in this approach as not all businesses are members of such organisations.

7. The weakness of the regulatory regime under Section 12(2) tends to mean that imported remedies may follow whichever standards are applicable in the country of origin. These vary widely.

8. The use of herbal medicines provides a popular alternative to 'orthodox' medicines. As highlighted in the House of Lords Select Committee's report on complementary and alternative medicine[2], 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 are close to the food/medicine borderline. However, a nationally representative random telephone survey of 1204 British adults, commissioned by the BBC in 1999, showed 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. Additionally, a report prepared for industry in 1999 on over-the-counter sales showed that around £50 million had been spent of herbal medicines. This report also suggested that sales of OTC complementary and alternative medicines were increasing. These reports indicate that herbal remedies are used by a large number of the UK population and that the use of herbal medicines is likely to

[2] The House of Lords Science and Technology Report on Complementary and Alternative Medicine Nov 2000.

continue to grow. Any growth in industry remains vulnerable to adverse publicity arising from issues over the safety and quality of remedies.

Identifying options

9. On the issue of whether there should be a Directive in the first place there are in principle various broad options:

- Option 1 - Continue to rely on existing controls, including Section 12(2) scheme (while opposing the introduction of a Directive)

- Option 2 - Introduce new UK scheme for herbal medicines *within* existing medicines regime (while opposing the introduction of a Directive)

- Option 3 - Introduce a new UK scheme for herbals *outside* existing medicines regime, combined with adjusting in a liberal direction UK interpretation of EU definition of what is a medicine (whilst also opposing the introduction of a Directive)

- Option 4 - Repeal Section 12(2) herbal exemption. Pending introduction of the proposed Directive, require all herbal medicines to meet the requirements applicable to medicines with a marketing authorisation. Subsequently transpose the Directive into UK law

- Option 5 - Transpose the proposed Directive into UK law. Repeal or disapply Section 12(2) subject to a transitional period.

Assuming the Directive goes forward, there is a further option as to its coverage.

- Option 6 - Extend coverage to at least some traditional medicines containing non- herbal active ingredients.

10. There are various further regulatory issues arising from the detailed terms of the proposed Directive. In the main, however, these cannot readily be categorised for distinct options.

Issues of equity and fairness as between current position and Option 5

11. Vulnerable members of society should not be adversely affected. Systematic provisions for information to the consumer under Option 5 could better protect those with serious illness from exaggerated claims sometimes made for unlicensed herbal remedies.

12. 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 5 should address this problem by requiring consistent standards, thereby achieving a more level playing field

- some companies may be concerned that others take advantage of the weakness of Section 12(2) to put products on the market of indeterminate legal status (as to the regulatory category of the product). Option 5 should bring greater transparency and encourage business to make clear decisions about which regulatory regime they are seeking to follow

- companies which have invested resources into demonstrating the efficacy of a herbal medicine in order to achieve a marketing authorisation are concerned about unsubstantiated health claims sometimes currently made for some unlicensed medicines. Option 5, by allowing authorised (minor) claims with traditional medicines registrations should improve on the present unsatisfactory position which arises when companies try to get round the "no written claims" rule for S12(2)

- companies with licensed medicines having proven efficacy may be concerned that in future, under Option 5, other companies will be able to put indications for use without having to provide scientific evidence of efficacy. However, product information will make clear that the usage is based on tradition and the efficacy of the product is not proven.

13. MCA operates as a trading fund. Currently the regulatory activities which MCA undertakes in relation to unlicensed herbal medicines to protect public health do not generate income. Under Option 5 there should be a fairer and more transparent approach to meeting the costs MCA incurs on the regulation of herbal medicines.

Identifying the benefits

Option	***comparison of options***
1	No perceived benefit in terms of protecting public health, giving no incentive for responsible companies wishing to operate high standards. Would maximise consumer choice and no additional burdens would be placed on businesses. Continuing vulnerability of sector to health scares arising from low standards
2 & 3	Would result in legislation specifically tailored for the traditional medicines used in the UK, but there would be an issue as to whether the legislation was compatible with Community law. Option 3 would run counter to Government policy that herbal remedies should be appropriately regulated as medicines
4	High levels of consumer protection but very limited consumer choice until supplemented by the introduction of the traditional medicines Directive. Major adverse regulatory impact on some companies
5	Should provide a secure regime within medicines law for the regulation of traditional herbal medicines, with greater certainty for companies. Should provide appropriate levels of consumer protection whilst maintaining consumer choice. Likely to encourage gradual progress towards more harmonised Europe market for at least some products
6	Similar benefits as for Option 5, but including some additional products. The proposed Directive includes provision for a review by the Commission of the operation of the Directive including the possibility of extending traditional use registration to other categories of medicinal products. However, there appears to be little prospect of European agreement on the inclusion of additional categories *in advance* of such a review. There is risk that European disagreement over possible controversial elements to the proposed Directive could jeopardise achievement of the Government's stated objective of achieving a secure regulatory framework for traditional herbal medicines. In turn this could put public health at continuing risk and lead to a weakening of public confidence in herbal medicines through continuing evidence of poor quality standards in parts of the sector

Quantifying and valuing the benefits of the preferred Option (Option 5)

14. The following benefits are possible for option 5:-

- improved **public health protection** through appropriate safety and quality controls; reduced adverse effects and better traceability in the event of an adverse reaction
- the introduction of a **scheme officially recognising traditional medicines** should increase consumer confidence and recognition of these products, leading to increased sales
- as compared with the current Section 12(2) regime, products will be allowed to carry minor **written indications for use** which may again help to increase consumer confidence and promote sales
- substantial **business opportunities** – particularly for companies in the ethnic medicines sector (given the current lack of licensed medicines from this sector) which can meet the required quality standards
- a **secure legal home** for traditionally used medicines would be created within European medicines law, giving companies greater certainty to plan for the future
- some **reduction over time in the difficulties in trading in herbal remedies across the EU**
- a **more level playing field between companies** operating in different parts of the herbal medicines sector, implying a **removal of the current adverse incentives** for companies wishing to behave responsibly
- much **greater transparency in the regulatory framework** than is currently the case with the Section 12(2) regime.

Compliance costs for businesses, charities and voluntary organisations of preferred option

15. This proposal should not significantly affect charities or voluntary organisations.

16. The businesses affected would be those involved in the manufacturer, sale and supply of finished or OTC herbal medicines. These businesses vary very widely in size. A number in all parts of the unlicensed herbal medicines sector are relatively small, as is also the case in the licensed herbal medicines sector.

17. The Herbal Registration Forum – which represents a number of trade associations operating in this sector in the UK - has made inquiries and given MCA some initial estimates about company size:

Number of employees in Company	***Number of Companies***
Less than 10:	22
10 – 50:	13
50 – 250:	15
250+	5

18. The Forum report that, of these companies, 8 have indicated that they already hold a medicines Manufacturers Licence granted by the MCA and a further 15 use a contract manufacturer holding a Manufacturers Licence granted by the MCA.

19. The proposal is likely to have a major regulatory impact on a number of businesses, particularly manufacturers, but also in some cases importers, wholesalers and retailers.

20. It is likely to be difficult to provide overall quantified information as the impact on individual companies will vary very widely according to the specific circumstances.

21. The compliance costs for companies will fall into a number of broad categories:

- specific fees associated with the scheme, including manufacturers', wholesale dealers' and importers' licences, inspection of premises, where appropriate, and the fee for registration of a product
- the cost of preparing applications
- the cost of any adjustments in individual products to meet the terms of the Directive. There may be a number of products which are legally sold under Section 12(2) but which do not meet the terms of the proposed Directive, e.g. their safety profile is not. There will also be products where adjustments to the product are required in order to comply with the terms of the Directive
- the costs of meeting the appropriate quality standards. In some cases this may well require modification of premises in order to meet Good Manufacturing Standards practice and the acquisition of professionally trained staff.

22. A broad illustrative assessment of the ***relative*** regulatory impact on **manufacturers** is summarised in the table below:

Relative Regulatory impact	***Type of company***
Category 1. Very high	Company with no systematic quality standards or expertise putting large numbers of low value products on the market
Category 2. High	Company following reasonable standards but with no experience of documenting processes and exposing them to external scrutiny
Category 3. Medium	Company which already applies the principles of systematic and well documented quality control through the supply chain but in another regulatory environment, e.g. food
Category 4. Medium/low	Company which already voluntarily meets quality standards which apply to licensed herbal medicines but does not have direct experience of medicines licensing
Category 5. Medium/Low	Company with existing experience in securing marketing authorisations for non herbal medicines
Category 6. Low	Company with existing experience in securing marketing authorisations for herbal medicines

23. In practice many other factors would complicate or modify the position for individual companies. The economic position of a company in category 1 might be sufficiently adversely affected that they chose to move out of the sector altogether. A company in category 2 which operated predominately in a different regulatory sector might choose to leave the herbal medicines sector rather than prepare to meet the Directive for a very small or low value product range. Equally, companies in different categories might choose some form of co-operation or merger to pool their distinctive relative advantages and minimise their relative disadvantages.

24. The regulatory impact may be particularly significant for some TCM businesses due to the current variability and unreliability of quality standards in parts of the sector. There is evidence of uncontrolled use of ingredients in some finished TCM products, (whether these originate from China or elsewhere). The direct impact of the Directive will be modified for this part of the sector because a significant proportion of the TCM activity relates not to finished OTC remedies but to individual remedies made up following one to one consultations between practitioners and patients. These remedies will not be affected by the Directive and will continue to be covered principally by the provisions of Section 12(1) (the herbalists' exemption) (However, a separate review of Section 12(1) in progress is also likely to lead to a requirement for higher standards.)

25. Income and profitability, as well as costs, could be significantly affected by the Directive. The cost of products from some manufacturers may rise, principally as a result of meeting the necessary quality standards. However, overall there should be greater public confidence flowing from improved quality, safety and product information. The public may well regard the traditional use indications in a positive light. These factors should translate into improved sales, and more stability in the market.

26. Following a transitional period, manufacturers and retail outlets will no longer be able to sell herbal remedies exempt under Section 12(2) of the Medicines Act. A proportion of herbal products which cannot demonstrate efficacy (for a licensed medicines) or traditional use (for a traditionally registered medicine) or be legitimately covered under food, cosmetics or general consumer product law will not have a secure regulatory home and some existing products may be lost from the market. This possibility is a result of replacing a largely uncontrolled regime. It is likely however, that a substantial proportion of any products at risk in this way would be able to come within one of the relevant regulatory regimes if there was some adjustment in the products' ingredients, strength or claims. Business, and manufacturers in particular, will therefore need to plan ahead; and there will need to be close liaison between the MCA and trade associations during this period.

27. In general the MCA's view from visiting a number of typical **retail** outlets is that the regulatory impact of the Directive is likely to be somewhat lower in much of the retail sector. Although there will be exceptions to this position, MCA's understanding is that, for many retailers, herbal remedies currently constitute a relatively limited proportion of shelf space alongside other "natural health" products and consumer goods. Moreover, the retailer will have the option of switching between manufacturers and suppliers. Retailers should benefit from the much greater consistency in presentation of products, including greatly improved product information.

Transitional arrangements

28. Moving to the new arrangements will inevitably pose a considerable challenge for many companies, particularly manufacturers. There is likely to be a need for some companies to adjust their product range over a period to reflect the updated regulatory framework. The MCA will have detailed discussions with industry over the handling of these arrangements and the Government will seek to ensure during negotiations on the Directive that an adequate transition period is retained.

Fee structure of preferred option

29. As a trading fund, the MCA must recover the costs of running a traditional medicines scheme. The fee structure and levels adopted for this Directive will be put before Parliament following public consultation.

30. It is too early to assess the likely fee levels. However, levels should reflect the fact that companies would not be having to demonstrate efficacy. The MCA is aware that some companies will be at the smaller end of the spectrum and that many may have significant numbers of products. In negotiations on the Directive, the Government proposes to advocate a significant role for the operation of positive lists. In this situation there would be set parameters as to ingredients, product strengths, dosage and indications. Companies would not need to demonstrate either the traditional use or the safety of their medicines if they were covered by the positive lists. Lower fees may be feasible in this situation reflecting the reduced requirement for MCA assessment of applications. Demonstrating compliance with quality requirements will be a common feature of all applications. Without compromising the requirement for companies to meet the set standards the MCA will consider whether there are options for streamlining the submission and assessment of quality data.

Specific regulatory impact concerns already expressed by business

31. The MCA is aware of several concerns about regulatory impact which have been expressed by sectors of business during discussion of early drafts of the Directive

    - *will the definition of traditional use be drawn too tightly so that some herbal remedies which have a traditional basis will be unable to meet the definition of traditional use?*

32. MCA's current assessment is that the key to retaining suitable flexibility is that the Directive should permit reference not only to specific manufactured herbal remedies but also to authoritative literature about the various herbal traditions practised by herbalists in the UK, and elsewhere in the EU. The MCA's current assessment is that the proposed Directive would permit use of this kind of evidence. The main non-western herbal traditions (TCM and Ayurveda) represented in the UK have already been present in this country for more than the minimum 15 year period of EU usage specified in the proposals.

    - *will quality standards be applied that are inappropriate and too onerous for traditional herbal remedies?*

33. There are existing quality requirements and European guidelines which apply to licensed herbal medicines. These are met successfully by large numbers of companies including many that are at the smaller end of the spectrum. Licensed herbal and traditional herbal medicines will typically have very similar products characteristics and so it should be equally feasible for companies to meet these requirements. Quality guidelines are intended to be applied in a way that it is appropriate to the product under consideration and there is flexibility, which MCA is accustomed to using, to accept legitimate arguments from companies where it is not feasible to provide data in a particular circumstance. The guidelines should reflect the fact that quality relating to efficacy will be of lesser importance.

Consultation with small businesses: ''The Litmus Test''

34. Small businesses have been, and will continue to be, consulted through trade associations, a number of which include small independent companies in their membership.

35. Also, earlier in 2001, the Small Business Service (SBS) interviewed the owners of two small businesses to gauge initial views. Both businesses had heard about the proposal. One specialised in the sale of herbal and traditional medicines and was positive about the proposals. The owner saw potential benefits in products carrying indications and thought this might aid sales. He did not envisage an increase in the price of the products sold as they already met high quality standards. The second bought in products and produced small quantities of traditional Chinese medicines for sale. The owner considered regulation unnecessary as the products had been used for centuries.

Identifying any other costs

36. There will be substantial compliance costs for the MCA. Currently MCA 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 is no requirement for MCA to have detailed regulatory involvement with most unlicensed herbal remedies. There will be significant costs involved in setting up and then running a new regulatory scheme for traditional herbal medicines. There will need to be detailed estimates of workload and costs, and fee levels set accordingly to recover these costs.

Results of consultation

37. This assessment takes into account the informal discussions held so far with the herbal sector encompassing manufacturers, suppliers, retailers and herbalists. The results of consultation on this partial RIA will be included in the final RIA. There may also be one or more interim update of the RIA during the course of negotiations on the Directive.

Enforcement, Sanctions, Monitoring and Review

38. The regulatory arrangement will be enforced by the MCA 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 a risk.

39. Guidance (using 'Plain English') and publicity will be required to help industry understand the requirements of the legislation and gain voluntary compliance. This aspect will be particularly important given the inexperience of parts of the sector in working within a clear regulatory framework.

40. There will be liaison as necessary with local government enforcement authorities. In accordance with the Cabinet Office's Enforcement Concordat, national guidance will be produced explaining the enforcement policy of the Agency and the rights of companies, including quick affordable routes for appeal against any decisions made.

27 March 2002

Summary and recommendations

OPTION	COSTS	BENEFITS	RISKS
1	None	No perceived benefit in terms of protecting public health. Will maximise consumer choice and no additional burdens will be placed on businesses	Continuing weakness in public health protection. A positive decision to go down this route could *increase* risk to public health by further encouraging supply of products that fall far short of the normal safety/quality standards for medicines. Would hinder UK companies from increased trade with other Member States. Self – regulation would prove difficult and possibly ineffective due to lack of incentive for companies. Continuing lack of transparency in regulation. The UK's credibility in Europe could suffer as the UK has advocated the need for European regulation of traditionally used herbal medicines
2	Significant costs of a new scheme	Specific scheme tailored to UK needs	Would require primary legislation but with continuing uncertainty for companies over legal position. Could get overtaken by European Directive, leading to major confusion for all interested parties
3	Significant costs of a new scheme	Legislation specifically tailored for the traditional medicines used in the UK	Would require primary legislation and run counter to Government policy of regulating herbal remedies appropriately within medicine law. This position was also supported by the House of Lords Science and Technology Committee Report on Complementary and Alternative Medicines. There would be continuing uncertainty over legal position
4	Loss of trade for some companies	High levels of consumer protection	For some products companies would not be able to meet the requirements set out in Directive 2001/83/EC as to efficacy. Limited consumer choice during the interim period. Disjointed approach
5	Vary widely between companies – significant for companies currently not operating to high standards	Will provide a secure regulatory regime within medicines law for the control of traditionally used herbal medicines. Will provide appropriate levels of public health protection whilst maintaining consumer choice. Could increase consumer confidence and hence sales. Consumers will be able to distinguish officially recognised traditionally registered products from any on the 'grey' market. At present the public can only guess which unlicensed herbal medicines are made to a high standard. Could, over time, improve operation of single market	Some companies may not be able to meet the standards of quality and safety or demonstrate traditional use. Specific requirements of the Directive may rule out certain products and require them to be withdrawn or at least adjusted. Risk that some irresponsible operators will continue, but in the black/grey market. The transitional process to new arrangements could be complex

OPTION	COSTS	BENEFITS	RISKS
6	Vary widely between companies	As for option 5 but for a wider range of products	Unlikely to be achievable for start of Directive; (but may be possible later). Risk of delay or failure to secure agreement on Directive and eventual unsatisfactory outcome for traditional herbal remedies

Annex E

CONSULTATION LETTER MLX 283

To **Alison Daykin**
Room 16 - 132
Market Towers
1 Nine Elms Lane
London SW8 5NQ

From: _____
_____
_____
_____
_____
_____

Please delete as applicable

1. We have no comments to make on the proposals in MLX 283

2. We have comments on:

- the proposal for a Directive on traditional herbal medicinal products
- the partial regulatory impact assessment

3. Our comments are attached:

- our reply may be made freely available
- our reply is confidential
- our reply is partially confidential (indicate clearly in the text which part(s) are confidential