



To: All Interested Parties

Our Ref: MLX 312

20/06/2005

Dear Sir/Madam,

CONSULTATION LETTER MLX 312

LICENSING OF HOMEOPATHICS: PROPOSALS FOR A NEW NATIONAL RULES SCHEME, FOR A REVIEW OF PRODUCT LICENCES OF RIGHT AND TO EXPAND THE REMIT OF THE ADVISORY BOARD ON THE REGISTRATION OF HOMEOPATHIC PRODUCTS (ABRH)

Introduction

I am writing to seek your views on a proposed National Rules Scheme for homeopathic medicines under Article 16(2) of Directive 2001/83/EC, on the proposed review of Product Licences of Right (PLRs) and on the proposed expansion of the remit of the ABRH .

Summary

Currently homeopathic medicines are either licensed under the “Simplified Scheme” or have “product licenses of right”, having been on the market when the Medicines Act (1968) came into force. For applications for new licences for homeopathic products, Article 16(1) of Directive 2001/83/EEC provides that homeopathic products which do not qualify for the simplified registration scheme must be authorised and labelled in accordance with the requirements for full marketing authorisations, including the provisions regarding proof of therapeutic effect. However, under Article 16(2) ‘A Member State may introduce or retain in its territory, specific rules for the pre-clinical tests and clinical trials of homeopathic products other than those referred to in Article 14(1) in accordance with the principles and characteristics of homeopathy as practised in that Member State’. These are the so-called ‘National Rules’ and it is this scheme the MHRA is proposing to introduce.

The rules would apply to all homeopathic products including those not eligible for the simplified registration scheme – for example parenteral products. Products would be licensed under the scheme with indications. Applications for authorisation of these products under the proposed scheme would need to be supported by a dossier of data on quality and safety together with appropriate product labelling and product literature and, it is proposed, bibliographic evidence that the product has been used in the indications sought.

Applicants would not be required to submit rigorous clinical data to demonstrate safety or efficacy. Therefore, it is proposed that indications for minor, self-limiting conditions only, would be admissible under the scheme.

It is also proposed that the MHRA will review product licences of right (PLRs) with a view to encouraging industry to re-register them, where appropriate, under the Simplified or new National Rules Scheme. It is also proposed that the MHRA will review the safety and efficacy of PLRs which are licensed for more serious indications. The proposed National Rules Scheme will be in addition to the existing Simplified Scheme, which will remain in place.

The ABRH was set up to give advice with respect to safety and quality in relation to any homeopathic medicinal product for human use in respect of which an application for the grant or renewal of a certificate of registration has been made or the licensing authority proposes to suspend or revoke the certificate of registration or homeopathic veterinary product which satisfies the conditions set out in Article 7 of the veterinary Homeopathic Directive (92/74/EEC). It is proposed to expand the remit of the Committee to include giving advice with respect to safety, quality and efficacy on any homeopathic medicinal product for human use in respect of which a marketing authorisation could be granted under Article 16.2 of Directive 2001/83/EC and on homeopathic medicinal products with PLRs.

Consultation

The regulation of homeopathic medicines impacts on a wide range of stakeholders. They include patients and patient groups, the homeopathic industry and healthcare professionals. MHRA is committed to involving views from as many interested parties as possible. If you know of other organisations that might have views that have been omitted from this consultation (list at Annex 3), please forward this letter or contact us so that we can send a consultation pack.

Timetable

Subject to the outcome of this consultation and agreement by Ministers, we propose to introduce the new National Rules Scheme on or shortly after 1 January 2006 (following the implementation of amending Directive 2004/27/EC).

Making copies available to the public

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 MHRA intends to make copies of comments received publicly available. Copies will be available shortly after the public consultation has ended.

The MHRA's Information Centre at Market Towers will supply these copies on request. An administrative charge, to cover the cost of photocopying and postage may be applied. Copies may be further reproduced. Alternatively, personal callers can inspect the replies at the Information Centre by appointment. To make an appointment, please telephone 020 7 084 2351.

Confidentiality

It will be assumed that your comments can be made publicly available unless you indicate 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 MHRA will not release confidential replies or replies containing personal confidential information.

Should you have any questions regarding the proposals outlined in this consultation, or the conduct of the consultation exercise, please contact Michael Darbyshire at the postal or e-mail address provided.

Comments

Any comments on these proposals should be sent to Mr. Michael Darbyshire **MHRA (Policy Projects Group) 16th Floor, Market Towers. 1 Nine Elms Lane, London SW8 5NQ** by no later than **12th September 2005.** You may also e-mail your response to michael.darbyshire@mhra.gsi.gov.uk. We regret that we cannot take comments over the telephone but you may send your comments by fax on the following number: 020-7084-2387. **Copies of replies will be made available to the public on request, unless you clearly state that you are replying “in confidence”. A reply proforma is attached at Annex 4**

Yours faithfully,



CONSULTATION DOCUMENT MLX 312

LICENSING OF HOMEOPATHICS: PROPOSALS FOR A NEW NATIONAL RULES SCHEME AND FOR A REVIEW OF PRODUCT LICENCES OF RIGHT.

LICENSING OF HOMEOPATHICS: PROPOSALS FOR A NEW NATIONAL RULES SCHEME AND FOR A REVIEW OF PRODUCT LICENCES OF RIGHT

Introduction

1. Under current licensing arrangements homeopathic products either have Product Licences of Right (PLRs), or have been granted certificates under the Simplified Scheme.
2. PLRs are licences that were issued to all products on the market at the time that the Medicines Act 1968 was implemented (in 1971). Homeopathic products covered by PLRs may have indications.
3. The Simplified Scheme was introduced in 1992 by Directive 92/73/EC. The procedure is regarded as simplified because there is no requirement for data to demonstrate efficacy and because the eligibility criteria confer a certain reassurance on safety so that the data requirements on safety are usually minimal. The Simplified Scheme does not allow indications
4. There is currently no procedure to enable new homeopathic products to be licensed with indications. As a result of this, there are inconsistencies in whether homeopathic products have indications, depending on when they were licensed.
5. These proposals are put forward to correct this anomalous situation and introduce a new scheme which would allow the marketing of homeopathic products with a limited range of indications that excludes serious diseases, such as cancer (Annex 2). The current simplified registration scheme would remain in place.
6. It is also proposed that the PLRs would remain in force, but that manufacturers would be encouraged to re-register their products currently licensed as PLRs, where appropriate, under the Simplified or National Rules Schemes. The MHRA would review PLRs with more serious indications.
7. Companies marketing homeopathic medicinal products also have the option of obtaining a full marketing authorisation for each product provided that the regulatory requirements for safety and efficacy of a medicinal product can be satisfied.

Background

8. PLRs are licences that were issued to all products on the market at the time that the Medicines Act 1968 was implemented (in 1971). It was intended that such products would, in time, be reviewed against current standards of quality safety and efficacy.

9. When the UK joined the European Community in 1973 European legislation came into force here and the review of those products covered by PLRs became mandatory. By the time of the Review it was recognised that providing proof of efficacy for homeopathic products would pose a difficulty if conventional clinical trials were required. Consequently homeopathic medicines were exempted from the Review and the PLRs remained in force.
10. At the time of the review, the requirement for proof of efficacy in clinical trials also meant that no new homeopathic products had been introduced onto the market since 1971. To resolve this situation, protracted negotiations in Europe led, in 1992, to the publication of Directives on human and veterinary homeopathic medicinal products that set out a 'simplified' regulatory procedure for homeopathic products that meet the following eligibility criteria:
 - The product must be prepared from products, substances or compositions called homeopathic stocks in accordance with homeopathic manufacturing procedure described by the European Pharmacopoeia or, in the absence of such a description, by any pharmacopoeia used officially in an EC member state.
 - It must be for oral or external use. (This includes all methods of administration except injections).
 - There must be no specific therapeutic indication included on the labelling or in any information relating to the product.
 - The product must bear the scientific name of the stock or stocks from which it is prepared and not a proprietary or trade name.
 - It must be sufficiently dilute to guarantee safety.
 - It must contain no more than one part per 10,000 of the mother tincture, and, where the active principle is a prescription only medicine (POM), it must contain no more than one part per 100 of the smallest dose used in allopathic medicine.
11. The procedure is regarded as simplified because there is no requirement for data to demonstrate efficacy (there are no indications) and because the eligibility criteria confer a certain reassurance on safety, so that the data requirements on safety are usually minimal.
12. The Directive relating to homeopathic products for human use has now been incorporated into Directive 2001/83/EC. Directive 2001/83/EC has recently been amended by Directive 2004/27/EC (see Annex 1 for the text of relevant provisions from Directive 2001/83/EC as amended). References in this consultation to Directive 2001/83/EC are to the Directive as amended.
13. Article 16(1) of Directive 2001/83/EC states that homeopathic products which do not qualify for the simplified registration scheme must be authorised and labelled in accordance with the requirements for full marketing authorisations, including the provisions regarding proof of therapeutic effect. However, Article 16(2) of the Directive allows member states to introduce specific rules for the pharmacological and toxicological tests and clinical trials of homeopathic products in accordance with the principles and characteristics of homeopathy as practised in that member state. These are the so-called 'National Rules'.

14. Companies marketing homeopathic medicinal products also have the option of obtaining a full marketing authorisation for each product providing that they can satisfy the requirements for demonstrating safety and efficacy set out in Directive 2001/83/EC. However, at present no homeopathic products are licensed with a marketing authorisation because of the difficulty of demonstrating efficacy under the rigorous conditions of controlled clinical trials.

The National Rules Scheme

General

15. It is proposed to make legislation under section 2(2) of the European Communities Act 1972 to introduce a National Rules Scheme in accordance with Article 16(2) of Directive 2001/83/EC. It should be noted that Article 16(2) only allows Member States to introduce an exemption from the requirements of Article 8(3)(i) of Directive 2001/83/EC i.e. the data that must be submitted in relation to safety and efficacy. All the other provisions of the Directive would apply to homeopathic medicinal products licensed under the National Rules scheme. (See sections 17-23 below for data requirements for homeopathic submissions under the National Rules Scheme).
16. Applicants should note in particular the pharmacovigilance obligations, including requirements for pharmacovigilance inspections (See Article 111 (1)(d) of Directive 2001/83/EC).

Advisory Board on the Registration of Homeopathic Products

17. The ABRH was set up to give advice with respect to safety and quality in relation to any homeopathic medicinal product for human use in respect of which an application for the grant or renewal of a certificate of registration has been made or the licensing authority proposes to suspend or revoke the certificate of registration or homeopathic veterinary product which satisfies the conditions set out in Article 7 of the veterinary Homeopathic Directive (92/74/EEC). It is proposed to expand the remit of the Committee to include giving advice with respect to safety, quality and efficacy on any homeopathic medicinal product for human use in respect of which a marketing authorisation could be granted under Article 16.2 of Directive 2001/83/EC and on homeopathic medicinal products with PLRs.

18. At present, if the licensing authority is minded to refuse an application for a certificate of registration an applicant can make representations to the ABRH, then the Medicines Commission and to a person appointed (the procedure is as set out in section 21 of the Medicines Act similarly in respect of compulsory revocation the procedure in schedule 2 to the Medicines Act applies). As part of the restructuring of the expert committees, it is proposed that holders/applicants for certificates will only make representations to the ABRH and then to a person appointed. This will also be the case with applications under the National Rules and the review of PLRs.
19. It is not proposed to change the membership of the ABRH.
20. It is proposed to amend the Medicines (Advisory Board on the Registration of Homoeopathic Products) Order 1995 by order under section 4 of the Medicines Act 1968.

Outline of Data Requirements

Quality

21. A complete dossier on the manufacture and control of the product would need to be submitted in line with requirements for other marketing authorisations. The usual requirements for manufacturer's licences and site inspection would apply. Compared with more dilute products, for those products more concentrated than the 1 in 10,000 (4x) limit currently applied, it is envisaged that additional in-process and finished product controls are likely to be needed to verify the content and uniformity of the homeopathic stock in the dosage form and any formulation master files already submitted will need to be revised. Quality requirements are laid out in Annex I to Directive 2001/83/EC.
22. An expert report on the quality dossier should also be provided.

Safety

23. Unlike the Simplified Scheme, in the proposed National Rules Scheme, the onus for supporting the safety of the product will lie with the applicant. The applicant would need to demonstrate the safety of the products given by the proposed route at the dilution(s) involved, by reference to relevant published literature or original data. Findings would need to be reflected in the labelling and Summary of Product Characteristics.
24. For those stocks which are derived from common food substances or are present in licensed medicines sold through general sales outlets, it is anticipated that a simple statement will be sufficient provided that the route of exposure is unchanged. As with the current registration scheme, stocks diluted to at least 1 in 10,000 of the mother tincture will have a general presumption of safety, except in cases where the stock is known to be toxic. It is proposed that the Agency will prepare and publicise a list of the stocks considered to be toxic and in respect of which applicants will need to supply additional data to support the safety of the products.
25. Nevertheless, in all cases, the applicant will still need to supply data to support the safety of the product and to justify the proposed product labelling and product literature. Such product literature would also need to be consistent with any

precautions or warnings appearing in literature for allopathic (conventional) products containing the same constituent unless differences could be justified on the grounds of dilution.

26. An expert report on the safety data should also be provided.
27. The safety of the product will then need to be monitored for the duration of the authorisation. Companies should be aware of the new pharmacovigilance requirements for electronic report of adverse reactions and submitting Periodic Safety Update Reports.

Efficacy

28. The applicant would need to provide suitable evidence that the product has been used as a homeopathic treatment in the indications sought. Information provided should be in the form of provings, excerpts from homeopathic *materia medica* or other bibliographic data and should be sufficient to demonstrate that homeopathic practitioners would accept the efficacy of the product for those indications.
29. As there are no requirements for rigorous clinical data to demonstrate efficacy, it is proposed that products would only be permitted to have indications for minor, self-limiting conditions. It is proposed to limit the scheme to products that are intended and designed for use in the treatment of minor, self-limiting conditions. Examples of indications that would be unacceptable are the treatment of malignant diseases, diabetes and other metabolic diseases, chronic insomnia, psychiatric conditions and cardiovascular diseases.
30. Typical examples of self-limiting conditions that could be covered be indicated for are travel sickness and nausea, headache, minor skin conditions, hay fever and other non-fatal allergies, common digestive disorders and muscular pain and stiffness (See Annex 2 for more examples of indications that might be permitted under the Scheme).
31. Applicants wishing to claim indications not admissible under these Rules would need

32. to apply for a full marketing authorisation supported by evidence of efficacy from controlled clinical trials.

Legal Status

33. The normal procedure of assigning a legal status would apply, so that all parenteral products would be Prescription only Medicines (POM).

Labelling and Product literature

34. The usual requirements for product labelling, the Patient Information Leaflet and Summary of Product Characteristics (SPC) would apply including the need for warnings and contraindications as appropriate. Companies should also be aware of the new requirements for consultations with patient groups, or “user testing”, on patient information leaflets. (See Article 59(3) set out in Annex 1
35. The authorisation number will be distinguished from full marketing authorisations (MAs) and Homeopathic Registration certificates (HRs), by using a specific prefix, possibly NR (National Rules certificates).

Fees

36. Companies wishing to register their products under the National Rules Scheme would have to pay a fee. It is proposed to consult on fees at a later date.

Product Licences of Right (PLRs)

37. A number of options for handling PLRs have been considered

- Option 1 Do nothing.
- Option 2 Revoke all PLRs by making legislation under Section 2 (2) of the European Communities Act 1972. The disadvantage of this option is that not all PLRs can be licensed under the New National Rules Scheme or under the existing Simplified Scheme, thus leaving some products without a regulatory home.
- Option 3 Re-licence all PLRs under the new National Rules Scheme. This was rejected because of the burden that it may have imposed on Industry, who would have to compile dossiers to support their products as well as pay fees to the MHRA to cover the cost of assessing their applications. This burden placed on industry was not thought to be justified by a public health gain.
- Option 4 PLRs are renewed and remain in force with the MHRA reviewing the indications that PLRs are currently licensed for. In particular the MHRA proposes reviewing PLRs licensed for more serious indications. Companies will be asked to consider varying their licences to remove these indications. There would be a beneficial effect of this approach for certain types of PLR product. Some of these products are so-called anthroposophic medicines and do not carry indications. (An anthroposophic medicine is a medicine prepared following homeopathic manufacturing procedures and prescribed based on the physical and spiritual features of a patient in accordance with the principles of Dr. Rudolf Steiner). It is not possible to register a product

under the National Rules Scheme without any therapeutic indication. Leaving these products as PLRs without indications will allow companies to retain them on the market for use in accordance with anthroposophic practice.

38. The MHRA considers Option 4 to be the best way forward. Further to this option, the MHRA proposes to encourage companies to consider applying for a new licence rather than renewing the PLR for products that are eligible under the Simplified or new National Rules Schemes. PLRs that do not 'fit' either scheme will be renewed and retained.
39. The proposals will help to correct the anomalous situation that the same product licensed as a PLR can have indications, whereas under the Simplified Scheme, it cannot. There will now be another scheme that also permits homeopathic products to have indications for minor self-limiting conditions. In addition the National Rules Scheme proposals will allow new products that are not eligible for the Simplified Registration Scheme and are not already marketed under a PLR to gain access to the market for the first time. Legislation enabling the products to be labelled with indications is also considered to be of significant benefit to patients.
40. An individual practitioner's ability to supply a product for whatever he feels fit, under his own responsibility, would not be affected by the proposals.

Procedures for PLRs

41. The licensing authority will review the indications that PLRs are licensed for in particular concentrating on products that are licensed for indications in more serious illnesses requiring constant clinical supervision. Companies will be asked to remove any indications if in the view of the licensing authority, that product can no longer safely be administered for the purposes indicated in the licence, or can no longer be regarded as efficacious for those purposes, and the company cannot reassure the licensing authority on these points. PLRs that are not eligible under the Simplified or New National Rules Schemes will be renewed in parallel with the indications review.
42. In the event that the licensing authority is not reassured regarding the continued use of the product for more serious illnesses, the licensing authority may consider compulsory variation of PLRs under the powers in Section 28 of the Medicines Act. The licensing authority is required to consult an appropriate Section 4 advisory committee, currently the Committee on the Safety of Medicines (CSM), before proposing compulsory variation of a licence. If the Committee is minded to advise the authority to vary a licence, the PLR holder would have a right to be heard by, or make written representations to the Committee before the Committee make their decision. It would be open to a PLR holder to apply for a marketing authorisation for their product for any indication that can be supported by appropriate efficacy data.

As set out in paragraph 18 above, it is proposed to expand the remit of the ABRH to include giving advice on the review and renewal of PLRs when required. Therefore, PLRs would be referred to the ABRH rather than to the CSM.

Guidance

43. Subject to consultation and agreement to go forward with the scheme, the MHRA will provide additional guidance to assist applicants in using the National Rules Scheme.

Comments

44. The MHRA would, therefore be grateful for your views, comments and suggestions on the proposals set out above, in particular:

- Do you agree with the basic proposals for the National Rules Scheme?
- Do you agree with the types of information listed to support the efficacy of homeopathic products?
- Do you agree that Option 4 is the best way to proceed with PLRs? If not, which option would you prefer and why?
- Do you agree with the proposals to only permit indications for minor self-limiting conditions under the scheme?
- Do you agree with the expanded remit of the ABRH?

45. A proforma for responses is at Annex 4, which you may return by post or e-mail no later **than 12th September 2005**.

**Selected Text from DIRECTIVE 2001/83/EC
as amended by
Directive 2004/24/EC as regards traditional herbal medicinal products, and
Directive 2004/27/EC**

Article 1 defines a *Homeopathic medicinal product* as follows:

Any medicinal product prepared from substances called homeopathic stocks in accordance with a homeopathic manufacturing procedure described by the European Pharmacopoeia or, in the absence thereof, by the pharmacopoeias currently used officially in the Member States. A homeopathic medicinal product may contain a number of principles.

CHAPTER 2 sets out the specific provisions applicable to homeopathic medicinal products:

Article 13

1. Member States shall ensure that homeopathic medicinal products manufactured and placed on the market within the Community are registered or authorised in accordance with Articles 14, 15 and 16, except where such medicinal products are covered by a registration or authorisation granted in accordance with national legislation on or before 31 December 1993. In case of registrations, Article 28 and Article 29(1) to (3) shall apply.

2. Member States shall establish a special simplified registration procedure for the homeopathic medicinal products referred to in Article 14.

Article 14

1. Only homeopathic medicinal products which satisfy all of the following conditions may be subject to a special, simplified registration procedure:

- they are administered orally or externally,
- no specific therapeutic indication appears on the labelling of the medicinal product or in any information relating thereto,
- there is a sufficient degree of dilution to guarantee the safety of the medicinal product; in particular, the medicinal product may not contain either more than one part per 10 000 of the mother tincture or more than 1/100th of the smallest dose used in allopathy with regard to active substances whose presence in an allopathic medicinal product results in the obligation to submit a doctor's prescription.

If new scientific evidence so warrants, the Commission may amend the third indent of the first subparagraph by the procedure referred to in Article 121(2).

At the time of registration, Member States shall determine the classification for the dispensing of the medicinal product.

The criteria and rules of procedure provided for in Article 4(4), Article 17(1) and Articles 22 to 26, 112, 116 and 125 shall apply by analogy to the special, simplified registration procedure for homeopathic medicinal products, with the exception of the proof of therapeutic efficacy.

Article 15

An application for special, simplified registration may cover a series of medicinal products derived from the same homeopathic stock or stocks. The following documents shall be included with the application in order to demonstrate, in particular, the pharmaceutical quality and the batch-to-batch homogeneity of the products concerned:

- scientific name or other name given in a pharmacopoeia of the homeopathic stock or stocks, together with a statement of the various routes of administration, pharmaceutical forms and degree of dilution to be registered,
- dossier describing how the homeopathic stock or stocks is/are obtained and controlled, and justifying its/their homeopathic use, on the basis of an adequate bibliography,
- manufacturing and control file for each pharmaceutical form and a description of the method of dilution and potentization,
- manufacturing authorization for the medicinal product concerned,
- copies of any registrations or authorizations obtained for the same medicinal product in other Member States,
- one or more mock-ups of the outer packaging and the immediate packaging of the medicinal products to be registered,
- data concerning the stability of the medicinal product.

Article 16

1. Homeopathic medicinal products other than those referred to in Article 14(1) shall be authorized and labelled in accordance with Articles 8, 10, 10a, 10b, 10c and 11.

2. A Member State may introduce or retain in its territory specific rules for the pre-clinical tests and clinical trials of homeopathic medicinal products other than those referred to in Article 14(1) in accordance with the principles and characteristics of homeopathy as practised in that Member State.

In this case, the Member State concerned shall notify the Commission of the specific rules in force.

3. Title IX shall apply to homeopathic medicinal products, with the exception of those referred to in Article 14(1).

TITLE V sets out the LABELLING AND PACKAGE LEAFLET requirements for all products. These will apply to homoeopathic products licensed under the National rules scheme. The requirements are as follows:

Article 54

The following particulars shall appear on the outer packaging of medicinal products or, where there is no outer packaging, on the immediate packaging:

- (a). the name of the medicinal product followed by its strength and pharmaceutical form, and, if appropriate, whether it is intended for babies, children or adults; where the product contains up to three active substances, the international non-proprietary name (INN) shall be included, or, if one does not exist, the common name;
- (b) a statement of the active substances expressed qualitatively and quantitatively per dosage unit or according to the form of administration for a given volume or weight, using their common names;
- (c). the pharmaceutical form and the contents by weight, by volume or by number of doses of the product;
- (d) a list of those excipients known to have a recognized action or effect and included in the detailed guidance published pursuant to Article 65. However, if the product is injectable, or a topical or eye preparation, all excipients must be stated;
- (e) the method of administration and, if necessary, the route of administration. Space shall be provided for the prescribed dose to be indicated;
- (f) a special warning that the medicinal product must be stored out of the reach and sight of children;
- (g) a special warning, if this is necessary for the medicinal product;
- (h) the expiry date in clear terms (month/year);
- (i) special storage precautions, if any;
- (j) specific precautions relating to the disposal of unused medicinal products or waste derived from medicinal products, where appropriate, as well as reference to any appropriate collection system in place;
- (k) the name and address of the marketing authorisation holder and, where applicable, the name of the representative appointed by the holder to represent him;
- (l) the number of the authorization for placing the medicinal product on the market;
- (m) the manufacturer's batch number;
- (n) in the case of non-prescription medicinal products, instructions for use.

Article 55

1. The particulars laid down in Article 54 shall appear on immediate packagings other than those referred to in paragraphs 2 and 3.

2. The following particulars at least shall appear on immediate packagings which take the form of blister packs and are placed in an outer packaging that complies with the requirements laid down in Articles 54 and 62:

- the name of the medicinal product as laid down in point (a) of Article 54,

- the name of the holder of the authorization for placing the product on the market,
- the expiry date,
- the batch number.

3. The following particulars at least shall appear on small immediate packaging units on which the particulars laid down in Articles 54 and 62 cannot be displayed:

- the name of the medicinal product as laid down in point (a) of Article 54 and, if necessary, the route of administration,
- the method of administration,
- the expiry date,
- the batch number,
- the contents by weight, by volume or by unit.

Article 56

The particulars referred to in Articles 54, 55 and 62 shall be easily legible, clearly comprehensible and indelible.

Article 56a

The name of the medicinal product, as referred to in Article 54, point (a) must also be expressed in Braille format on the packaging. The marketing authorisation holder shall ensure that the package information leaflet is made available on request from patients' organisations in formats appropriate for the blind and partially sighted.

Article 57

Notwithstanding Article 60, Member States may require the use of certain forms of labelling of the medicinal product making it possible to ascertain:

- the price of the medicinal product,
- the reimbursement conditions of social security organizations,
- the legal status for supply to the patient, in accordance with Title VI,
- identification and authenticity.

For medicinal products authorised under Regulation (EC) No 726/2004, Member States shall, when applying this Article, observe the detailed guidance referred to in Article 65 of this Directive.

Article 58

The inclusion in the packaging of all medicinal products of a package leaflet shall be obligatory unless all the information required by Articles 59 and 62 is directly conveyed on the outer packaging or on the immediate packaging.

Article 59

1. The package leaflet shall be drawn up in accordance with the summary of the product characteristics; it shall include, in the following order:

(a) for the identification of the medicinal product:

(i) the name of the medicinal product followed by its strength and pharmaceutical form, and, if appropriate, whether it is intended for babies, children or adults. The common name shall be included where the product contains only one active substance and if its name is an invented name;

(ii) the pharmaco-therapeutic group or type of activity in terms easily comprehensible for the patient;

(b) the therapeutic indications;

(c) a list of information which is necessary before the medicinal product is taken:

(i) contra-indications;

(ii) appropriate precautions for use;

(iii) forms of interaction with other medicinal products and other forms of interaction (e.g. alcohol, tobacco, foodstuffs) which may affect the action of the medicinal product;

(iv) special warnings;

(d) the necessary and usual instructions for proper use, and in particular:

(i) the dosage,

(ii) the method and, if necessary, route of administration;

(iii) the frequency of administration, specifying if necessary the appropriate time at which the medicinal product may or must be administered; and, as appropriate, depending on the nature of the product;

(iv) the duration of treatment, where it should be limited;

(v) the action to be taken in case of an overdose (such as symptoms, emergency procedures);

(vi) what to do when one or more doses have not been taken;

(vii) indication, if necessary, of the risk of withdrawal effects;

(viii) a specific recommendation to consult the doctor or the pharmacist, as appropriate, for any clarification on the use of the product;

(e) a description of the adverse reactions which may occur under normal use of the medicinal product and, if necessary, the action to be taken in such a case; the patient should be expressly asked to communicate any adverse reaction which is not mentioned in the package leaflet to his doctor or pharmacist;

(f) a reference to the expiry date indicated on the label, with:

(i) a warning against using the product after that date;

(ii) where appropriate, special storage precautions;

(iii) if necessary, a warning concerning certain visible signs of deterioration;

(iv) the full qualitative composition (in active substances and excipients) and the quantitative composition in active substances, using common names, for each presentation of the medicinal product;

(v) for each presentation of the product, the pharmaceutical form and content in weight, volume or units of dosage;

(vi) the name and address of the marketing authorisation holder and, where applicable, the name of his appointed representatives in the Member States;

(vii) the name and address of the manufacturer;

(g) where the medicinal product is authorised in accordance with Articles 28 to 39 under different names in the Member States concerned, a list of the names authorised in each Member State; (h) the date on which the package leaflet was last revised.

2. The list set out in point (c) of paragraph 1 shall:

(a) take into account the particular condition of certain categories of users (children, pregnant or breastfeeding women, the elderly, persons with specific pathological conditions);

(b) mention, if appropriate, possible effects on the ability to drive vehicles or to operate machinery;

(c) list those excipients knowledge of which is important for the safe and effective use of the medicinal product and which are included in the detailed guidance published pursuant to Article 65.

3. The package leaflet shall reflect the results of consultations with target patient groups to ensure that it is legible, clear and easy to use.

Article 60

Member States may not prohibit or impede the placing on the market of medicinal products within their territory on grounds connected with labelling or the package leaflet where these comply with the requirements of this Title.

Article 61

1. One or more mock-ups of the outer packaging and the immediate packaging of a medicinal product, together with the draft package leaflet, shall be submitted to the authorities competent for authorising marketing when the marketing authorisation is requested. The results of assessments carried out in cooperation with target patient groups shall also be provided to the competent authority.
2. The competent authority shall refuse the marketing authorization if the labelling or the package leaflet do not comply with the provisions of this Title or if they are not in accordance with the particulars listed in the summary of product characteristics.
3. All proposed changes to an aspect of the labelling or the package leaflet covered by this Title and not connected with the summary of product characteristics shall be submitted to the authorities competent for authorizing marketing. If the competent authorities have not opposed a proposed change within 90 days following the introduction of the request, the applicant may put the change into effect.
4. The fact that the competent authority does not refuse a marketing authorization pursuant to paragraph 2 or a change to the labelling or the package leaflet pursuant to paragraph 3 does not alter the general legal liability of the manufacturer and the marketing authorization holder.

Article 62

The outer packaging and the package leaflet may include symbols or pictograms designed to clarify certain information mentioned in Articles 54 and 59(1) and other information compatible with the summary of the product characteristics which is useful for the patient, to the exclusion of any element of a promotional nature.

Article 63

1. The particulars for labelling listed in Articles 54, 59 and 62 shall appear in the official language or languages of the Member State where the product is placed on the market. The first subparagraph shall not prevent these particulars from being indicated in several languages, provided that the same particulars appear in all the languages used. In the case of certain orphan medicinal products, the particulars listed in Article 54 may, on reasoned request, appear in only one of the official languages of the Community.
2. The package leaflet must be written and designed to be clear and understandable, enabling the users to act appropriately, when necessary with the help of health professionals. The package leaflet must be clearly legible in the official language or languages of the Member State in which the medicinal product is placed on the market.

The first subparagraph shall not prevent the package leaflet from being printed in several languages, provided that the same information is given in all the languages used.

3. When the product is not intended to be delivered directly to the patient, the competent authorities may grant an exemption to the obligation that certain particulars should appear on the labelling and in the package leaflet and that the leaflet must be in the official language or languages of the Member State in which the product is placed on the market.

Article 64

Where the provisions of this Title are not complied with, and a notice served on the person concerned has remained without effect, the competent authorities of the Member States may suspend the marketing authorization, until the labelling and the package leaflet of the medicinal product in question have been made to comply with the requirements of this Title.

Article 65

In consultation with the Member States and the parties concerned, the Commission shall draw up and publish detailed guidance concerning in particular:

- (a) the wording of certain special warnings for certain categories of medicinal products;
- (b) the particular information needs relating to non-prescription medicinal products;
- (c) the legibility of particulars on the labelling and package leaflet;
- (d) the methods for the identification and authentication of medicinal products;
- (e) the list of excipients which must feature on the labelling of medicinal products and the way in which these excipients must be indicated;
- (f) harmonised provisions for the implementation of Article 57.

Article 66

1. The outer carton and the container of medicinal products containing radionuclides shall be labelled in accordance with the regulations for the safe transport of radioactive materials laid down by the International Atomic Energy Agency. Moreover, the labelling shall comply with the provisions set out in paragraphs 2 and 3.

2. The label on the shielding shall include the particulars mentioned in Article 54. In addition, the labelling on the shielding shall explain in full, the codings used on the vial and shall indicate, where necessary, for a given time and date, the amount of radioactivity per dose or per vial and the number of capsules, or, for liquids, the number of millilitres in the container.

3. The vial shall be labelled with the following information:

- the name or code of the medicinal product, including the name or chemical symbol of the radionuclide,
- the batch identification and expiry date,
- the international symbol for radioactivity,
- the name and address of the manufacturer,

- the amount of radioactivity as specified in paragraph 2.

Article 67

The competent authority shall ensure that a detailed instruction leaflet is enclosed with the packaging of radiopharmaceuticals, radionuclide generators, radionuclide kits or radionuclide precursors. The text of this leaflet shall be established in accordance with the provisions of Article 59. In addition, the leaflet shall include any precautions to be taken by the user and the patient during the preparation and administration of the medicinal product and special precautions for the disposal of the packaging and its unused contents.

Article 68

Without prejudice to the provisions of Article 69, homeopathic medicinal products shall be labelled in accordance with the provisions of this title and shall be identified by a reference on their labels, in clear and legible form, to their homeopathic nature.

Article 69

1. In addition to the clear mention of the words 'homeopathic medicinal product', the labelling and, where appropriate, the package insert for the medicinal products referred to in Article 14(1) shall bear the following, and no other, information:

- the scientific name of the stock or stocks followed by the degree of dilution, making use of the symbols of the pharmacopoeia used in accordance with Article 1(5); if the homeopathic medicinal product is composed of two or more stocks, the scientific names of the stocks on the labelling may be supplemented by an invented name,
- name and address of the registration holder and, where appropriate, of the manufacturer,
- method of administration and, if necessary, route,
- expiry date, in clear terms (month, year),
- pharmaceutical form,
- contents of the sales presentation,
- special storage precautions, if any,
- a special warning if necessary for the medicinal product,
- manufacturer's batch number,
- registration number,
- 'homeopathic medicinal product without approved therapeutic indications',
- a warning advising the user to consult a doctor if the symptoms persist.

2. Notwithstanding paragraph 1, Member States may require the use of certain types of labelling in order to show:

- the price of the medicinal product,
- the conditions for refunds by social security bodies.

Examples of indications that might be permitted under the National Rules Scheme

System or part of the body or disease	Permitted use:
1. The cardio-vascular system.	<p>‘symptomatic relief of’:</p> <p>Chilblains.</p> <p>Haemorrhoids by relief of symptoms by means of locally effective preparations or stool softening agents and lubricants.</p>
2. The endocrine system.	<p>Weight reduction dependent upon mechanism involving a reduced calorie or joule intake.</p>
3. The gastro-intestinal system.	<p>‘symptomatic relief of’:</p> <p>Indigestion, heart burn, hyperacidity, dyspepsia, halitosis (bad breath) or flatulence.</p> <p>Colicky pain, stomach ache or nausea.</p> <p>Occasional or non-persistent diarrhoea or constipation.</p> <p>Travel sickness or related symptoms.</p>
4. The genito-urinary system and mammary glands.	<p>‘symptomatic relief of’:</p> <p>Dysmenorrhea.</p> <p>Sore nipples during lactation by means of local applications.</p>
5. Infections including viral, bacterial and fungal diseases.	<p>‘symptomatic relief of’:</p> <p>Minor cutaneous infections where a medicinal product is to be administered to an external surface of the body, including treatment by means of preparations for the relief of pruritus or exanthematous rashes of childhood infection and treatment of boils and the treatment or</p>

	<p>prevention of athlete's foot.</p> <p>Apthous ulcers.</p> <p>Common colds, coughs, conditions commonly referred to as influenza and similar upper respiratory tract infections.</p> <p>Minor acute inflammatory conditions of the buccal cavity and pharynx.</p>
6. The musculo-skeletal system.	<p>'symptomatic relief of':</p> <p>Muscular pain and stiffness including backache, sciatica, lumbago, fibrositis, rheumatic pain and cramp.</p>
7. The nervous system.	<p>'symptomatic relief of':</p> <p>Headache including migrainous headache.</p> <p>Neuralgia.</p> <p>Difficulties falling asleep</p> <p>Agitation, anxiety, irritability, nervous tension, stresses, strains, tenseness</p>
8. The optical and auditory system.	<p>'symptomatic relief of':</p> <p>by means of the local administration of eye preparations.</p>
9. Parasitic disease	Head Lice
10. The respiratory system.	<p>'symptomatic relief of':</p> <p>Hay fever, rhinitis or catarrh.</p> <p>Blocked-up sinuses.</p>

11. The skin, hair and scalp.	<p>‘symptomatic relief of’:</p> <p>Where applied to an external surface of the body, of acne.</p> <p>Dandruff by means of external applications.</p> <p>Psoriasis by application to an external surface of the body.</p> <p>Where applied to an external surface of the body, of eczema and skin allergies.</p> <p>Hard skin and corns</p> <p>Contact dermatitis by means of protective applications.</p> <p>Common minor skin conditions including dry and chapped skin, cold sores, nettle rashes, pruritus, insect bites and napkin rash.</p>
12. The teeth and gums.	<p>‘symptomatic relief of’:</p> <p>Gingivitis and pyorrhoea by means of oral hygiene.</p>

CONSULTATION LIST

Alliance of Registered Homeopaths.
Anthroposophic Medical Association
Anthroposphical Association
Arthritis Care
Association of British Health Care Industries
Association of British Neurologists
Association of the British Pharmaceutical Industry
Association of Clinical Research in the Pharmaceutical Industry
Association of Community Health Councils of England & Wales
Association of Hospice Management
Association of Independent Multiple Pharmacies
Association of Palliative Medicine
Association of Pharmaceutical Importers
Association of Traditional Chinese Medicine UK
Association of Veterinarians in Industry
Association for Nurse Prescribing
Association for sick Children
ATC
Ayurvedic Medical Association UK
Ayurvedic Trade Association
Asthma & Allergy Research
Back Care
BBSRC
Biohealth Ltd
Boiron Ltd (Irene Chetcuti)
Breakthrough Breast Cancer
Breast Cancer Care
British Acupuncture Council
British Association of Anthroposophic Pharmacists
British Association for Nutritional Therapists
British Association of Dermatologists
BASFAM
British Association of Pharmaceutical Physicians
British Association of Pharmaceutical Wholesalers
British Chiropody and Podiatry Association
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 Geriatric Association
British Herb Trade Association
British Herbal Medicines Association
British Homoeopathic Association
British Institute of Regulatory Affairs
British International Doctors' Association
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 Osteopathic Association
British Pharmacological Society
British Society for Allergy and Clinical Immunology
British Society for Rheumatology
British Society of Gastroenterology
British Veterinary Association
British Advisory Centres
BAAAP
Cancer BACUP
Cancer Research Campaign
Cancer Research UK
CARE
CCCPH
CEMVO
Central Medical Advisory Committee
CHAI
Chemist & Druggist
Chinese Competent Authority
Chinese Medical Institute & Register
CMAS
College of Pharmacy Practice
Committee on Advertising Practice
Commonwealth Working Group on Traditional and Complementary Health
Community Pharmacy Magazine
Community Pharmacy Wales
Community Practitioners and Health Visitors Association
Community Services Pharmacists Group
Consolidated Communications
Consumers Association
Consumers in Europe
Consumers for Health Choice
Council for Alternative and Complementary Medicine
Council for the Professions Supplementary to Medicine
Court Service
CPHVA
Department of Health
Department of Health and Social Services (NI)
Dispensing Doctors Association
Doctor Magazine
Drug & Therapeutics Bulletin
Drug Information Pharmacists Group
Drug Safety Research Unit
DTI
Essential Oil Trade Association
European Association of Hospital Pharmacists
European Council for Classical Homoeopaths
European Herbal Practitioners' Association
Faculty of Homoeopathy
Faculty of Pharmaceutical Medicine
Foundation for Integrated Medicine
General Medical Council
General Practitioners Committee
General Practitioners Committee (Wales)
General Practitioners Association (NI)
George Lewith
Guild of Healthcare Pharmacists
HCSA
Health Development Agency

Health Food Institute
Health Food Manufacturer's Association
Health Professions Council
Health Protection Agency
Health Service Commissioner
Health Which?
Homeopathic Trust
IHRC
Imperial Cancer Research Fund
Independent Healthcare Association
Internal Holistic Aromatherapy Foundation
International Federation of Aromatherapists
International Society of Pharmacovigilance
Irish Veterinary Association
Local Authority Central Office of Trading Standards (LACOTS)
Macmillan Cancer Charity
Medical Defence Union
Medical Defence Union (Scotland)
Medical Protection Society Ltd
Medical Research Council
Medicines Commission
National Association of Health Stores
National Association of Women Pharmacists
National Back Pain Association
National Board for Nursing, Midwifery & Health Visiting (NI)
National Consumer Council
NCHSPCS
National Eczema Society
National Institute of Medical Herbalists
National Patient Safety Agency
National Pharmaceutical Association
Natural Medicines Manufacturers' Association UK
Natural Medicines Society
NCH & SPCS
Neonatal and Paediatric Pharmacists Group
NHS Information Authority (Coding & Classification)
NICE
NMMA
Northern Ireland Consumer Council
Nursing and Midwifery Council
OTC Bulletin
OTC Business News (Informa Publishing Group Ltd)
OTC News & Market Report
Paediatric Chief Pharmacists Group
Pain Concern UK
Pain Relief Foundation
The Pain Society
Patients Association
Patients Association for Anthroposophic Medicine
Paul Geoghegan
PECFI
Penny Viner
Pharmaceutical Journal
Pharmaceutical Quality Group
Prescription Medicines Code of Practice Authority
Primary and Community Care Pharmacy
Proprietary Association of Great Britain
Prostate Cancer Charity
Register for Chinese Herbal Medicine
Royal Botanic Gardens
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 Pharmaceutical Society of Great Britain
Royal Pharmaceutical Society of Great Britain (Scotland)
Royal Pharmaceutical Society of Great Britain (Welsh Executive)
Royal Society for the Promotion of Health
Scottish Consumer Council
Scottish Deans Medical Curriculum Group
Scottish General Practitioners Committee
Scottish Pharmaceutical Federation
Scrip Ltd
Skin Care Campaign
Small Business Service
Society of Homoeopaths
Society of Pharmaceutical Medicine
Society for the Promotion of Nutritional Therapy
SSIPH
Switch
TAPASI
British Society for Allergy
The Herb Society
The Institute for Complementary Medicine
The Society of Chiropractors and Podiatrists
UK Inter-Professional Group
Third Sector
Tic-Tac Administration
Tutshells Enterprise IG
UK Clinical Pharmacy Association
UK Gout Society
UK Homoeopathic Medical Association
UK Inter-Professional Group
UK-DURG Administrator
Unified Register of Herbal Practitioners
Veterinary Medicines Directorate (VMD)
Welsh Consumer Council
WNB NMHV

Annex 4

RESPONSE TO CONSULTATION LETTER MLX 312

LICENSING OF HOMEOPATHICS: PROPOSALS FOR A NEW NATIONAL RULES SCHEME

Please complete the proforma and return to Michael Darbyshire MHRA (Policy Projects Group) 16th Floor, Market Towers, 1 Nine Elms Lane, London SW8 5NQ by 12th September 2005. You may also e-mail your response to michael.darbyshire@mhra.gsi.gov.uk

Name:

Company name:.....

We have the following comments to make on proposals for the Homeopathic National Rules Scheme:

(Please use additional sheets as required)

DRAFT PARTIAL REGULATORY IMPACT ASSESSMENT**1. TITLE**

Proposals for a specific UK National Rules Scheme for licensing homeopathic medicinal products under Article 16(2) of Directive 2001/83 EEC as amended by Directive 2004/27/EC and for a review of existing Product Licences of Right (PLRs).

2. PURPOSE AND INTENDED EFFECT OF THE MEASURE**2.1 Objective**

To address the current inconsistencies in the way that homeopathic products are marketed in the UK in order to create a level playing field. This will be achieved by introducing a National Rules Scheme under Article 16.2 of Directive 2001/83 and reviewing Product Licences of Right.

Currently, homeopathic products have either “Product Licences of Right”, having been on the market when the Medicines Act (1968) came into force, or are registered under the “Simplified Scheme”, which was introduced in 1992 by Directive 92/73/EC.

The key difference between the two current schemes is that products licensed with Product Licences of Right (PLRs) may have therapeutic indications i.e. their label names the disease(s) the product may be used to treat, whereas those introduced by the Simplified Scheme are not permitted to have indications under Directive 2001/83 because of the difficulty in demonstration efficacy by clinical trials. PLRs are licences that were issued to all products on the market at the time that the Medicines Act 1968 was implemented (in 1971).

We want to remove these inconsistencies by allowing applicants to market a range of products with indications, whilst ensuring that standards of safety and quality are met. This will strengthen the public health protection of users of homeopathic medicinal products.

2.2 Background

The Medicines Act 1968 was implemented in the UK in 1971 and all medicinal products currently on the UK market, including homeopathic products, were given Product Licences of Right (PLRs). It was intended to review PLRs against current standards of quality safety and efficacy. In 1973, the UK joined the EU, European legislation came into force and the review of PLRs became mandatory.

By the time of the Review it became obvious that proof of efficacy for homeopathic products would be difficult if clinical trials were required and homeopathics were therefore, exempted from the review and PLRs remain in force. Currently almost 3,000 PLRs are extant.

The requirement for proof of efficacy meant that it was not possible to introduce new homeopathic medicinal products onto the market. After much discussion in Europe, Directive 92/73 was implemented in 1992 in order to resolve the efficacy issues.

Thus, under current licensing arrangements homeopathic products either have Product Licences of Right (PLRs), or have been granted certificates under the Simplified Scheme.

The Simplified Scheme was introduced in 1992 by Directive 92/73/EC. The procedure is regarded as simplified because there is no requirement for data to demonstrate efficacy and because the eligibility criteria confer a certain reassurance on safety so that the data requirements on safety are usually minimal. The Simplified Scheme does not allow indications, but homeopathic products covered by PLRs may have indications.

Although there has always been scope, both under Directive 92/73 and under 2001/83, to set up a specific rules scheme within the UK, there is currently no procedure to enable new homeopathic products to be licensed with indications and there are, therefore, inconsistencies in whether homeopathic products have indications, depending on when they were licensed.

As a result, some manufacturers are able to market a wider range of dosage forms and dilutions and give indications for their products while others are not permitted to do so. This has the effect of creating barriers to equal access to the market and differences in the information available to users of these products. There are almost 3000 products that are currently allowed in a wide range of presentations and permitted to give indications. In addition, there are approximately 200 products which are not permitted to have indications because they have been registered more recently under the Simplified Scheme.

It is proposed that the National Rules Scheme will come into effect after 1 January 2006. The scheme is optional and there is, therefore, no transition period necessary. The proposed PLR review time scale is five years.

Our proposals will benefit both the general public, by strengthening the public health protection of users of homeopathic medicinal products and the homeopathic industry by levelling the playing field and increasing the range of products that can be marketed. The associated increase in costs for MHRA and the homeopathic industry are offset against the benefits outlined above.

2.3 Risk Assessment

The risk of leaving things is that the expansion of the homeopathic industry will be inhibited by the prevention of the development of new products with indications.

Currently, there are cases where two identical products are available, one with indications and one without, depending on whether or not the product was marketed prior to the medicines Act (1968) coming into force. This difference in the information available to users of homeopathic medicines causes the risk of patient confusion.

3. OPTIONS

Four options have been identified, encapsulating the implementation of the National Rules Scheme (including the handling of PLRs):

- Option 1 Do nothing. This was rejected as the present inequalities would continue. While there are no strong public health reasons for taking action, this option is not attractive. Sections of the homeopathic industry are known to be discontented with the current situation and are likely to pursue the issue.
- Option 2 Revoke all PLRs by making legislation under Section 2 (2) of the

European Communities Act 1972. This was rejected as not all PLRs can be licensed under the New National Rules Scheme or under the existing Simplified Scheme, thus leaving some products without a regulatory home.

- Option 3 Introduce a National Rules Scheme which would allow applicants to market a wider range of products and to claim therapeutic indications. Applicants would need to provide a full quality dossier in line with the requirements of Annex 1 of Directive 2001/83 and demonstrate the safety of the products given by the proposed route at the dilution(s) involved, by reference to relevant published literature or original data. In terms of efficacy, the applicant would need to provide suitable evidence that the product has been used as a homeopathic treatment in the indications sought. Information provided should be in the form of provings, excerpts from homeopathic *materia medica* or other bibliographic data and should be sufficient to demonstrate that homeopathic practitioners would accept the efficacy of the product for those indications.

Option 4 Introduce a Scheme as in Option 2, but take the further step of rationalising the regulatory system for those products by ensuring that existing products (i.e. PLRs) comply with the proposed licensing arrangements, particularly in terms of their indications. Companies will be encouraged to re-register PLRs under either the National Rules or the Simplified Schemes on a voluntary basis. PLRs for products which companies do not wish to re-register or which are not eligible for the newer schemes will be reviewed in terms of indications and renewed. As there will be no requirement to submit rigorous clinical data to demonstrate safety or efficacy, it is proposed that indications for minor, self-limiting conditions only, would be acceptable at review. Companies will be asked to remove any indications if in the view of the licensing authority, that product can no longer safely be administered for the purposes indicated in the licence, or can no longer be regarded as efficacious for those purposes, and the company cannot reassure the licensing authority on these points. Companies will be given every opportunity to support proposed indications. An individual practitioner's ability to supply a product for whatever he feels fit, under his own responsibility, would not be affected by the proposals.

Renewal will be carried out under the existing legislation of the Medicines Act and may require the submission of additional data.

4. BENEFITS

- Option 1 No benefits for business or people using homeopathic medicinal products, the present inequalities will continue.
- Option 2 No benefits for business as not all PLRs can be authorised under the new National Rules Scheme or registered under the existing Simplified Scheme, leaving some products without a regulatory home.
- Option 3 This option would mean that users of homeopathic medicinal products will have access to products marketed with consistent patient information with competition between manufacturers on an equal footing. The industry as a whole will benefit from the opportunity to gain indications for products for which use within the homeopathic tradition can be demonstrated, but cannot currently carry indications. In addressing equal access to the market, those manufacturers who previously had the advantage of being able to claim indications while others could not, will lose that advantage.

In addition the National Rules Scheme proposals will allow new products that are not eligible for the Simplified Registration Scheme and are not already marketed under a PLR to gain access to the market for the first time. Legislation enabling the products to be labelled with indications is also considered to be of significant benefit to patients. Improving market access will increase competition and therefore, reduce prices

Informal discussions with representatives of the homeopathic sector suggest that the proposals for the National Rules Scheme would be well received.

Option 4 As for Option 3. In addition, there would be a beneficial effect of this approach for certain types of PLR product. PLRs for products which companies do not wish to re-register or which are not eligible for the newer schemes will be reviewed in terms of indications and renewed

Some of these products are so-called anthroposophic medicines and do not carry indications. (An anthroposophic medicine is a medicine prepared following homeopathic manufacturing procedures and prescribed based on the physical and spiritual features of a patient in accordance with the principles of Dr. Rudolf Steiner). It is not possible to register a product under the National Rules Scheme without any therapeutic indication. Leaving these products as PLRs without indications will allow companies to retain them on the market for use in accordance with anthroposophic practice.

Reviewing the PLRs will provide an opportunity to rectify any cases where products are being marketed with inappropriate indications.

4.1 Business Sectors Affected

The only business sector directly affected is the homeopathic medicines manufacturing industry.

There are currently four major UK companies (NelsonBach, Weleda, Ainsworth and Helios), but it is expected that companies from other Member States, some of whom currently market homeopathic products registered under the Simplified Scheme in the UK, will wish to licence products under the National Rules Scheme. In a report published by Mintel (Complementary Medicines in the UK, Market Intelligence, March 2003), the most recent figures available, it was estimated that the market for homeopathic remedies in the UK was around £29m in 2002.

5. COMPLIANCE COSTS

5.1 Compliance Costs for Business

A summary of the costs to the industry and to the MHRA can be found below. No substantive environmental or social costs have been identified in relation to the proposed scheme. Further information on the nature of these costs can be found in the narrative below the table.

	Ongoing costs to industry	Other costs to industry	Ongoing costs to MHRA	Other costs to MHRA
Option 1	£0	£0	£0	£0
Option 2	£410 per PLR re-	£2,444 per ML	£216,000	£0

	registered.					
Option 3	£350.- £1,219 per product	per	£1,250-£5,000 dossier	per	£216,000 annum	per £0
			£2,444 per ML			
Option 4	£350 - £1,219 per product.	per	£1,250-£5,000 dossier	per	£216,000 annum	per £0
	£410 per PLR.		£2,444 per ML			

Option 1 (Do nothing)

No direct figurable cost to business. However, unequal access to the market may impact on competition between manufacturers, and could keep prices artificially high for those products which legitimately carry indications. Only manufacturers applying the current registration scheme incur the costs of application fees and the cost of compiling dossiers.

Option 2 (Revoke all PLRs)

Applicants would pay a fee for each product previously covered by a PLR to be registered under the Simplified Scheme or authorised under the National Rules Scheme. This option would result in products which do not “fit” under either scheme being lost to the market.

Option 3: (new national rules allowing indications)

Option 3 would give manufacturers of registered homeopathic products an additional option to apply for a licence that would allow therapeutic claims to be made. If they chose not to, there would be no cost involved. MHRA would charge a fee for assessing an application for a licence and as with all fees charged by the Agency, this would be set at a level to reflect the work actually carried out. The current fee for a registration under the Simplified Scheme (without indications) varies between £134 and £869 per product, depending (amongst other things) on whether the product or a similar one has been assessed by the Agency before. A similar scale of fees could be used for the assessment of products under the new scheme but with an additional element for the assessment of data provided for indications. This element of the work would cost in the region of say £350 (options: £300, £400) per product i.e. giving a total fee between £484 and £1,219.

Option 4: (levelling the playing field by voluntarily re-registering PLRs in the new scheme and the existing registration scheme and reviewing and renewing those that do not ‘fit’ either scheme)

The costs associated with the implementation of Option 3 would be the same as for Option 2 above. Priority will be given to reviewing existing Product Licences of Right with serious indications and this would involve around 1000 PLRs which would be subject to the fees within 5 years after implementation.

The additional cost to this sector of the industry in a five-year period would be:
1000 (number of PLRs that may need to be reviewed)

the fee for reviewing PLR (which has been calculated as £134, based on a survey of MHRA records for PLRs)

plus

a proportion of the annual fee and a renewal fee.

Using these costs, the likely total cost to the Industry in a five year period is £134,000 plus a proportion of the annual fee and a renewal fee.

An annual fee would be payable set at the same level as that for a Registration Certificate (currently £15 per product). In addition, a fee would be payable at the renewal of the licence after 5 years.

This means that the additional cost to this sector of the industry in a five-year period would be 3000 (total number of PLRs) x the average fee (which has been calculated as £410, based on a survey of MHRA records for PLRs) plus a proportion of the annual fee and a renewal fee.

Estimates of fees that could be charged for applications under the National Rules Scheme and for the review of PLRs are given in section 7 below .

Other costs

In addition to the application fees there will be other ‘once only’ costs associated with making an application:

- **Compilation of dossiers:** No information is available on the cost of compiling a dossier for homeopathic medicinal products. Depending on whether or not the product is currently registered or licensed, little or no new technical information will need to be generated for the application dossiers. Based on this fact, it is suggested that the average cost of the dossiers will be similar to that of a simple abridged application for a marketing authorisation for a conventional medicinal product which was estimated to be about £1,250. The cost is likely to vary considerably from lower than the average figure, if the cost is spread over several applications using the same data generated from one application, to costs which could rise as high as £5,000 in some cases if complexities arose, for example, in a few cases where generation of additional technical data may be required.
- **Manufacturer’s licences (MLs).** Companies which do not already hold an ML will need to obtain one. The current fee for an ML is £2,444 for a standard licence and £142 for a non-orthodox practitioner’s licence. Currently, it is not possible to estimate how many new companies will apply under the National Rules Scheme, but further information will be obtained once the proposed pre-submission notification scheme is implemented in the second quarter of 2005. .
- **Revision of labelling:** There will also be costs to the generation of revised labelling and product information, including user testing for existing authorised products. We do not hold information on the cost of revising labelling and product information nor on the cost of user testing and would welcome consultees’ cost estimates of what they think this will mean to their business per product.

A full public fees consultation will take place in the second quarter of 2005 to seek views on proposals to introduce or amend fees in this area.

There is no cost to local authorities or to the NHS. .

There is no cost on the environment nor are there any social costs.

Cost to the MHRA are estimated at £216,000 per annum.

7. Costs for a typical business

It is not possible to estimate this at present as a suitable 'typical' business does not exist

There is the option for companies holding registrations for homeopathic medicines obtained under the Simplified Scheme already in existence to apply for authorisations for these products under the New National Rules Scheme. Such applications will attract a reduced fee, say £350 per product as quality and safety aspects will have already been addressed and only efficacy issues will need to be assessed.

Thus a small business with applications for two products will pay £700 in fees, a medium business with thirty products will pay £10,500 and a large business with 70 products £24,500. There will be the additional cost of assembling the evidence for use in the indications sought. An annual fee would be payable set at the same level as that for Registration Certificate (currently £15 per product), and in addition, a fee would be payable at the renewal of the licence after 5 years.

Applications for products not previously registered under the Simplified Scheme will attract a higher fee, as quality and safety assessments will need to be carried out. Using the same number of applications as above and assuming that the products contain more than five homeopathic stocks which have not previously been seen by the licensing Authority, (such applications attract the highest fees of, say, £1219 per application), the fees would be £2,438 for the small company, £36,570 for the medium company and £85,330 for the large company. Annual and renewal fees would be the same as above. It is assumed that applicants will phase their initial applications to avoid a large financial outlay for fees and other costs.

8.: Consultation with small business

Informal consultation has taken place with key industry representative associations and with experts in the field of homeopathic practice over the past three years. They have been broadly supportive of the proposed scheme because it will enable them to market a wider range of products and products with indications.

We intend to consult widely, with all holders of PLRs and HRs (including companies of varying size). The responses to the consultation will further inform the final RIA.

9. Competition Assessment

The competition filter test has been carried out in relation to homeopathic companies both in the UK and in other EU member States and suggests that a full assessment is not required, a simple competition assessment being sufficient.

The affected market will be the over-the-counter medicines sector. Currently only homeopathic medicines with PLRs are labelled with indications for their use. (The majority of these are held by three companies. Implementation of the National Rules Scheme will enable all companies to market more products with indications. This will increase consumer choice and ensure equal access to the market. The National Rules Scheme is voluntary and

its costs will depend on the number of products a company wishes to authorise. The number of companies with homeopathic authorisations is likely to increase. Some of the companies concerned already hold registration certificates granted under the Simplified Scheme and will have the option of re-applying for homeopathic authorisations under the National Rules Scheme, which will enable them to market these products with indications..

10. Enforcement and Sanctions

Enforcement and control of the legislation will be achieved within the existing enforcement mechanisms i.e. Schedule 3 of the Marketing Authorisation Regulations . Offences in the Marketing Authorisation regulations will be relevant as all the requirements of directive 2001/83/EC will apply to products licensed under the National Rules Scheme. Penalties imposed on summary conviction of such an offence, are a fine not exceeding £5,000 or an indictment to a fine or imprisonment for not more than two years.

11. Monitoring and Review

Initially, applications received will be monitored on a monthly basis and regular meetings with stakeholders and trade associations will be used to monitor the effectiveness and success of the new scheme. The regulations will be reviewed in three years time. The associated fees regulations will be reviewed annually.

12. Consultation

We have consulted informally with Industry representatives and leaders in the field of homeopathic practice and intend to consult formally with trade associations, professional bodies, patient groups and holders of both Product Licences of Right and holders of Registration Certificates. A positive response to the proposals was received from all parties consulted informally. Those consulted will be asked for views on the cost compliance of the scheme, including a small business litmus test.

12.1 Fairness Issues

The Medicines and Healthcare products Regulatory Agency (MHRA) would like consultees to consider and answer the following questions:

- Is it fair to perpetuate inconsistencies in the way homeopathic products are marketed for no reason other than differences in the licensing regime when they were first licensed/registered resulting in disadvantage to companies wishing to enter or expand the UK market and thus limiting the choice of consumers?
- Is it fair to remove existing serious indications from a product which is currently marketed when data to support its efficacy are lacking?
- Is it fair that users of homeopathic medicinal products are confused by products that are similar (or the same) being sold in different ways?
- Is it fair to increase the regulatory burden on manufacturers of existing products to ensure equal access to markets?

Is it acceptable for a large number of existing products to continue to be marketed without ever having had to demonstrate satisfactory quality and safety and justify claims for therapeutic efficacy?

13. Summary and Recommendations

Of the four options identified, Option 1 (do nothing) would not address the current inconsistencies in the marketing of products, which lead to inequity in marketing and confusion to users of these products. Option 2 (revoke all PLRs) would result in products which do not “fit” under either of the newer schemes having to be withdrawn from the market. Option 3 (new National Rules allowing indications) would allow access to a market with indications for use, which has not been possible since 1971. It would not, however, create equity in the market since some of the provisions of the new scheme would not be consistent with the provisions of the Product Licence of Right system. Option 4 (levelling the playing field by re-registering PLRs in the new scheme and the existing registration scheme) has the advantages of Option 2 and will also create a level playing field for the industry. In addition, users of these products will have consistent information. We consider that the costs to both the MHRA and the homeopathic companies associated with setting up and operating systems under this option are outweighed by the benefits to both the homeopathic industry and to public health. Thus the MHRA recommends the adoption of Option 4.

Declaration:

I have read the Regulatory Impact Assessment and am satisfied that the balance between cost and benefit is the right one in the circumstances.

Signed by the responsible Minister:

Date:

Contact Point for this RIA:

Michael Darbyshire, MHRA (Policy Projects Group) 16th Floor, Market Towers. 1 Nine Elms Lane, London SW8 5NQ michael.darbyshire@mhra.gsi.gov.uk