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To: interested organisations

17 January 2000

Dear Sir or Madam

CONSULTATION LETTER MLX 258: FURTHER PROPOSALS TO PROTECT THE PUBLIC FROM UNLICENSED MEDICINES CONTAINING HERBAL INGREDIENTS AT RISK OF CONFUSION WITH *ARISTOLOCHIA* SPECIES

Please find attached consultation document MLX 258. You are invited to comment on the proposals and a form is attached for your reply. Comments or queries should be addressed to Paul Brittain in room 619 at the above address, **to arrive by 17 February 2000.**

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

The Agency’s Information Centre at Market Towers will supply copies upon request. Copies may be further reproduced. An administrative charge, to cover the costs 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 0171 273 0351.

We will assume that your comments can be made publicly available in this way 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 Agency will not release confidential replies or replies containing personal confidential information.

Yours faithfully,

Richard Woodfield
Group Manager

CONSULTATION DOCUMENT MLX 258

Further proposals to protect the public from unlicensed medicines containing herbal ingredients at risk of confusion with *Aristolochia* species

INTRODUCTION

1. Regulatory action has already been taken to protect the public from unlicensed medicines containing toxic *Aristolochia* species. This consultation is about further proposals to protect the public from exposure to a number of specific herbal ingredients which, although not believed to be inherently harmful, are at risk of being confused with *Aristolochia* species.
2. In July 1999 the Medicines Control Agency (MCA) consulted on proposals to prohibit the import, sale or supply of unlicensed medicines presented as containing herbal ingredients at risk of being confused with *Aristolochia* species (MLX 254-see Annex 1). In the light of that consultation, of a sampling and analysis exercise by the MCA, and of advice from the Committee on Safety of Medicines (CSM), Ministers are minded to take regulatory action to deal with herbal ingredients at risk of confusion with *Aristolochia* species. The proposed action is set out in the attached Order (Annex 2). Because there are elements of the proposals which go beyond those in MLX 254 there is now a further short period of consultation.

BACKGROUND

3. MLX 254 provided information about the regulation of herbal medicines in the UK and the risk to health from *Aristolochia* species. A number of named plants may be confused with *Aristolochia* species, either because they have similar common or Pin Yin names, or because in Chinese herbal tradition certain herbs with similar medicinal properties are interchangeable. MLX 254 also explained previous action taken in relation to *Aristolochia* species, and the need for further safeguards.
4. The Medicines (Aristolochia) (Emergency Prohibition) Order 1999 came into force on 28 July 1999. This was superseded by the Medicines (Aristolochia) (Temporary Prohibition) Order 1999 which continues in force until 30 June 2001.
5. Last year's consultation exercise showed wide support for the need for regulatory action against herbal ingredients at risk of confusion with *Aristolochia* species. There were mixed views as to whether an absolute prohibition was required or whether some form of conditional prohibition might suffice. In order to further assess the extent of the risk, alongside the consultation exercise the MCA carried out a sampling exercise of herbal ingredients known to be at risk of confusion with *Aristolochia* species. Of 63 samples, 28 (44%) were found to contain varying levels of aristolochic acids (indicating the presence of *Aristolochia* species), thus posing a very serious risk to public health.
6. The CSM has advised the need for an absolute prohibition of herbal ingredients at risk of being confused with *Aristolochia* species in unlicensed medicines. In the light of the disquieting results of the sampling and analysis

exercise, and the fact that there are no currently agreed arrangements across the Traditional Chinese Medicine (TCM) sector for ensuring the exclusion of *Aristolochia* species from unlicensed medicines, the Government is minded to accept that advice.

CONSULTATION ON FURTHER REGULATORY ACTION

7. The proposals in the Order include:

(a) An absolute prohibition on sale, supply and importation of any unlicensed medicine consisting of or containing any of the following herbal ingredients:

Akebia quinata

Akebia trifoliata

Clematis armandii

Clematis montana

Cocculus orbiculatus

Cocculus thunbergii

Cocculus trilobus

Stephania tetrandra

(b) An absolute prohibition on sale, supply and importation of any unlicensed medicine presented as consisting of or containing:

(i) any of the herbal ingredients listed above, or

(ii) *Mu Tong* or *Fangji*

8. The Order includes two changes from the proposals for an absolute prohibition of the herbal ingredients at risk of confusion with *Aristolochia* species set out in MLX 254. One is the inclusion of *Cocculus* species as plants at risk of being confused with *Aristolochia* species. The other proposes that the prohibition covers “consisting of or containing” as well as “presented as consisting of or containing” the named herbal ingredients at risk of being confused with *Aristolochia* species. These provisions would serve to enhance public protection.

9. Views are sought on the proposals set out in the Order, and in particular:

(i) *Cocculus* species to be included in the list of prohibited herbal ingredients

(ii) Prohibition on importation, sale or supply of unlicensed medicines to be extended to unlicensed medicines consisting of or containing herbal ingredients at risk of being confused with *Aristolochia* species.

FUTURE ACTION

10. The CSM has agreed to set up a working party to advise on whether any further action is required to make effective the prohibition of *Aristolochia* species, and under what conditions any prohibitions of herbal ingredients that were believed to

be harmless but easily confused with *Aristolochia* species might be lifted or modified without unacceptable risk to public health.

11. The MCA plans to establish a forum to address the need to improve safety and quality standards in ethnic medicines on the UK market, in particular in the TCM and Ayurvedic sectors. The forum will include representatives of the traditional Chinese medicine sector, the regulatory authorities and external parties. In the first instance the forum will concentrate on voluntary improvements in quality and safety standards and the work will proceed alongside the work the MCA is undertaking to address the need for improved statutory regulatory arrangements for unlicensed herbal medicines.

REGULATORY IMPACT

12. A draft regulatory impact assessment is at Annex 3. We recognise that businesses may incur some costs as a result of the extended prohibition. However, if effective regulatory action is not taken there could be considerable loss of public confidence in TCM, leading to significantly worse financial consequences for those involved in the sector.

13. Comments are invited on the regulatory impact of these proposals.

14. Subject to the outcome of consultation and the agreement of Ministers we propose to lay a Statutory Instrument in Parliament around the end of February 2000.

MCA
January 2000

To : Paul Brittain
Medicines Control Agency
Room 619 Market Towers
1 Nine Elms Lane
LONDON SW8 5NQ

From : _____

CONSULTATION LETTER MLX 258

**FURTHER PROPOSALS TO PROTECT THE PUBLIC FROM UNLICENSED
MEDICINES CONTAINING HERBAL INGREDIENTS AT RISK OF
CONFUSION WITH *ARISTOLOCHIA* SPECIES**

- * 1. We have no comment to make on the proposals in MLX 258.
- * 2. Our comments on the proposals in MLX 258 are below/attached.
 - * *My reply may be made freely available.*
 - * *My reply is confidential.*
 - * *My reply is partially confidential (indicate clearly in the text any confidential elements)*

Signed : _____

* *Delete as appropriate*

CONSULTATION DOCUMENT MLX 254

Proposals to protect the public from unlicensed medicines containing the herbal ingredient *Aristolochia*

INTRODUCTION

1. This consultation document sets out proposals to make an order under Section 62 of the 1968 Medicines Act prohibiting the import, sale or supply of unlicensed medicinal products containing any plant of the genus *Aristolochia*. The proposed prohibition is in the interests of public safety. (It would serve to make permanent a temporary order which takes effect from 28 July). Views are invited on the proposals and also on options for regulatory action in relation to a number of other herbal ingredients. These are not of themselves harmful, but there is some evidence of a risk that an unlicensed product presented as having any of these ingredients may contain *Aristolochia* as an undeclared ingredient. The Medicines Commission and the Committee on the Safety of Medicines (CSM) support the need for regulatory action to give the public more systematic protection from *Aristolochia*.

BACKGROUND

(a) Regulation of herbal medicines in the United Kingdom

2. There are two regulatory routes by which herbal medicines can reach the UK market:

- *unlicensed herbal remedies* do not have to meet any set safety or quality standards
- *licensed herbal medicines* have to satisfy rigorous standards of evidence on safety, quality and efficacy – on the same basis as other licensed medicines.

The Government's stated objective is that the public should have continuing access to a wide range of safe and high quality herbal remedies with appropriate information about the use of the products. In support of this objective, the Medicines Control Agency (MCA) is currently holding constructive informal discussions with a wide range of interest groups from across the natural health sector to explore the possibility of moving towards regulatory arrangements which provide a more effective balance between consumer safety and consumer choice. Any such broader developments will take some while - and are likely to depend on agreement in the European Union. The MCA will be contributing positively in ongoing EU discussions about herbal medicines.

*(b) The risk to health from *Aristolochia**

3. *Aristolochia* has a longstanding use as an ingredient in Traditional Chinese Medicine (TCM). However, **it is now very widely accepted in the scientific community that aristolochic acids, contained in *Aristolochia* species, pose serious risks to health – they are mutagenic, carcinogenic and have been shown to damage the kidneys.** The most serious recorded incident occurred in Belgium in the early 1990s when around 80 women were reported to have become ill with kidney damage as a result of taking a slimming product where *Aristolochia* had been substituted for *Stephania*. Some of the women subsequently required renal transplants.

(c) The use of Pin Yin names in TCM

4. TCM herbal ingredients are often traded using “Pin Yin” names. These are not specific botanical names but are descriptions of the colour, shape, taste or odour of the herbal ingredients, or they may describe the actions or uses. It is common practice in this herbal tradition to substitute one herbal ingredient with another reputedly having similar medicinal properties, even though it may be botanically unrelated. Another issue is that unrelated Pin Yin names can be phonetically very similar.

*(d) Homoeopathic products containing *Aristolochia**

5. There is also a tradition of use of *Aristolochia* in homoeopathy. At extreme levels of dilution, *Aristolochia* poses no measurable risk to public health. **Accordingly, in line with the advice of CSM, none of the proposals in this consultation would affect any licensed or registered homoeopathic products.**

PREVIOUS ACTION TAKEN TO PROTECT THE UK PUBLIC

6. A number of EU member states have taken action through bans or other measures to protect the public from the hazards presented by *Aristolochia*. In the UK, the following measures have been taken so far:

- in 1997, the MCA carried out a sample of unlicensed medicines presented as containing *Stephania*. The (undeclared) ingredient *Aristolochia* was detected in a high proportion of cases. The MCA then warned known importers of TCM that *Stephania* was at risk of contamination or substitution with *Aristolochia*. On account of the risk posed by the latter, these importers agreed that they would no longer supply *Stephania*
- a follow up spot check of a number of TCM outlets was carried out by the MCA. This detected no products presented as containing either *Aristolochia* or *Stephania*
- in 1997 *Aristolochia* was made a prescription only medicine (POM). This meant that only a medical practitioner could legally prescribe a medicine containing *Aristolochia*. (However, an exemption from the POM Order applies to products containing a dilution of at least one part in a million (6x))

- in July 1998 the MCA repeated its warning to TCM businesses and organizations representing practitioners about the need for vigilance to prevent *Aristolochia* reaching the market
- on a wider level the MCA instigated dialogue with the Chinese regulatory authorities in 1998 to address the issue of the variable quality of some TCM products entering the UK. The MCA has also encouraged the development of self regulation within the UK TCM sector.

THE NEED FOR FURTHER SAFEGUARDS

7. Two cases have recently been reported in the UK where there is evidence that serious kidney damage suffered by patients was associated with the presence of *Aristolochia* in unlicensed medicinal products. The MCA's investigation of these cases has highlighted a continuing risk that *Aristolochia* may find its way into the supply chain. The serious threat to the health of any person taking a medicine containing *Aristolochia* is such that firm and prompt regulatory action is justified to back up measures previously taken.

8. There are several specific factors pointing to a continuing risk from the **unintended** inclusion of *Aristolochia* in herbal medicines:

- **risk of confusion between similar Pin Yin names** This is likely to be responsible for at least some of cases where *Aristolochia fangchi* (Pin Yin name: "Guang Fangji") has been mistakenly used in place of *Stephania tetrandrda* (Pin Yin name: "Han Fangji"). The MCA understands that, while the use of *Stephania* has reduced considerably following the earlier initiative by the Agency, some herbalists still continue to use this herbal ingredient. There is likely to be a risk that not all such supplies are currently subject to adequate authentication and quality control
- **interchangeability of herbal ingredients:** The Pin Yin name "Mu Tong" is applied to a range of alternative herbal ingredients. Most of these are harmless, however one possible alternative is a species of *Aristolochia* (*A manshuriensis*). There are also a number of patent medicines where Mu Tong would be an expected ingredient. Overall, this suggests that, in principle, there could be a risk that *Aristolochia* may, from time to time, enter the supply chain in products presented as containing Mu Tong. There is evidence that both of the *Aristolochia* incidents which the MCA is currently investigating have had their origin in confusion over the ingredients of Mu Tong
- **economic pressures** At an international level the increase in popularity of herbal remedies has meant that for some herbal species the demand may outstrip the availability of authenticated, good quality supplies. It is possible that a minority of operators in the TCM sector may have taken advantage of the current lack of a systematic UK regulatory framework for ensuring the safety and quality of unlicensed herbal remedies. The development of self regulation in this sector is currently still at a relatively early stage.

9. An additional reason for taking further regulatory action is that the previous designation of *Aristolochia* as a POM does not prevent a doctor from **intentionally** prescribing this herbal ingredient. Given the widely reported dangers, this would be likely to happen in practice only rarely if at all. However, it is undesirable in principle that the possibility should be left open.

CONSULTATION ON FURTHER REGULATORY ACTION

(a) *Aristolochia*

10. **On the advice of the CSM, an urgent temporary order is to be made prohibiting the sale, supply and importation from non EU member states of medicinal products containing the herbal ingredient *Aristolochia*. This order will come into force on 28 July and will run for 3 months.**

11. **Views are sought on the proposal that this prohibition should be made permanent.**

(b) *Other herbal ingredients at risk of being confused with Aristolochia*

12. There is a difficult balance to be struck. It is clearly undesirable in principle to prohibit the use of ingredients which are considered to be inherently harmless. However, the over-riding concern must be to protect public health. **The MCA's aim therefore would be to minimise the scope of any further prohibitions *provided that an effective way can be found to safeguard public health*.** On this basis, comments are invited on two alternative approaches:

Option 1: prohibition, by order, on the sale, supply or importation of any unlicensed medicine presented as containing any of the following herbal ingredients:

**Stephania
Fangji
Mu Tong
Clematis armandii*
Clematis montana*
Akebia quinata*
Akebia trifoliata***

**these are herbal ingredients to which the Pin Yin name Mu Tong is commonly applied*

13. There is already considerable evidence from the UK, and internationally, that products presented as containing *Stephania* are prone to contamination or substitution with *Aristolochia*. There is currently much less direct evidence that products purporting to contain Mu Tong, or any the four herbs to which the name Mu Tong is commonly applied, are in practice significantly prone to include *Aristolochia*. However, such evidence as exists is relatively recent and comes from the UK. During

the consultation period the MCA will continue to investigate whether there is further evidence on this issue.

Option 2: prohibition, by order, as in Option 1. However, the order would specify that the prohibition would be conditional and would *not* apply where the person placing the product on the market exercised due diligence to ensure that the product did not contain *Aristolochia*. (The MCA would need to provide guidance on its view as to what constituted due diligence. Ultimately this would be a matter for the courts to decide.)

14. The MCA would look to the TCM sector, during the consultation period, to put forward an informed view on what practical measures could be put in place quickly by TCM businesses and practitioners, as necessary, which would serve to demonstrate that due diligence had been taken to ensure that a medicinal product presented as containing the specified herbs did not contain *Aristolochia*. After dialogue with the TCM sector the MCA would then reach a view on (a) whether the approach of a conditional prohibition was feasible and (b) if so, the nature of the guidance as to action required to demonstrate due diligence.

15. It may be that in the short term it is more readily feasible to give the necessary quality assurance to the public where the product consists of wholly or largely unprocessed ingredients than would be the case for patent products where ingredients are more highly processed. Factors such as these would be taken into account by the MCA in working up final proposals.

16. Views are invited on the relative merits of Options 1 and 2. If respondents favour Option 2, views are invited on what specific measures the public are entitled to expect businesses and/or practitioners to take to demonstrate that due diligence has been exercised to ensure that products presented as containing any of the various named herbs do not in fact contain *Aristolochia*. Views are also sought on which herbal ingredients should be covered by a prohibition or conditional prohibition.

REGULATORY IMPACT

17. A formal regulatory impact assessment will need to be prepared in the light of final proposals. *Aristolochia* is already a POM. The legal market in the UK for products containing this herbal ingredient is currently likely to be virtually non-existent. There would clearly be some potential loss of business in the TCM sector if medicines containing *Stephania* or Mu Tong were to be prohibited, as under Option 1. The MCA's understanding is that the loss of trade would be more of an issue in relation to Mu Tong than would be the case with *Stephania*. It is possible that any loss of trade would be compensated in whole or in part by use of alternative TCM herbs.

18. The financial impact on business and practitioners of actions which might be required under Option 2 to demonstrate due diligence is difficult to assess at this stage. In principle, all responsible UK businesses and practitioners dealing in unlicensed medicines should **already** be operating rigorous quality assurance

themselves and/or purchasing supplies from reliable sources known to have such systems in place. There is a basic consumer expectation that when (s)he buys any consumer product, it should contain the ingredients stated on the label, that the product should be of suitable quality and should not be contaminated. To the extent that businesses in unlicensed herbal medicines are already following high standards, it may be argued that extending such standards to other business is helping to create a level playing field.

19. The overriding effect on business and practitioners of the proposed regulatory action, however, is likely to depend on public confidence. The key issue will be the extent to which the proposed regulatory action, combined with the practical response of the TCM sector, is sufficient to reassure the public that TCM products are safe and of acceptable quality.

20. The MCA will have further specific discussions with the TCM sector. **In the meantime, general views are invited on the regulatory impact of these proposals.**

21. Subject to the outcome of consultation and the agreement of Ministers we propose to implement the change by laying a Statutory Instrument in Parliament. The timing will depend on responses to the consultation and on the outcome of discussions with the TCM sector.

MCA
27 July 1999

STATUTORY INSTRUMENTS

2000 No.

MEDICINES

The Medicines (Mu Tong etc.) (Temporary Prohibition) Order 2000

<i>Made</i>	2000
<i>Laid before Parliament</i>	2000
<i>Coming into force</i>	2000

As respects England, Scotland and Wales, the Secretary of State concerned with health in England, and, as respects Northern Ireland, the Minister of Health, Social Services and Public Safety, acting jointly, in exercise of the powers conferred upon them by sections 62(1)(a) and (2) and 129(4) of the Medicines Act 1968 ⁽¹⁾ and now vested in them ⁽²⁾ and of all other powers enabling them in that behalf, it appearing to them to be necessary in the interests of safety to make the following Order, after consulting such organisations as appear to them to be representative of interests likely to be substantially affected by the Order pursuant to section 129(6) of that Act, and after consulting and taking into account the advice of the Committee on Safety of Medicines pursuant to sections 62(3) and 129(7) of that Act ⁽³⁾, hereby make the following Order:-

Citation, commencement, expiry and interpretation

1. - (1) This Order may be cited as the Medicines (Mu Tong etc.) (Temporary Prohibition) Order 2000, shall come into force on March 2000 and shall continue in force until the end of 30th June 2001, when it shall expire.

(2) In this Order –

¹ 1968 c. 67. The expressions “the appropriate Ministers” and “the Health Ministers” are defined in section 1 of that Act as amended by article 2(2) of, and Schedule 1 to, S. I. 1969/388.

² In the case of the Secretary of State concerned with health in England, by virtue of article 2(2) of, and Schedule 1 to, S.I. 1969/388, and articles 2(1) and 5 of, and paragraph 1(1) of the Schedule to, S.I. 1999/ ; and in the case of the Minister of Health, Social Services and Public Safety, by virtue of section 95(5) of, and paragraph 10 of Schedule 12 to, the Northern Ireland Act 1998 (c.47).

³ Section 62(3) refers to “the appropriate committee”, which is defined in section 4(6) of the Act. The Committee on Safety of Medicines was established under section 4 of the Act, by S. I. 1970/1257, for the purposes set out in that instrument.

“the Act” means the Medicines Act 1968;

“EEA Agreement” means the Agreement on the European Economic Area signed at Oporto on 2nd May 1992 (⁴) as adjusted by the Protocol signed at Brussels on 17th March 1993 (⁵);

“EEA State” means a State which is a Contracting Party to the EEA Agreement.

Prohibition of sale, supply and importation of any medicinal product consisting of or containing certain plants

2. Subject to article 4 below, the sale, supply and importation of any medicinal product consisting of or containing a plant (⁶) belonging to any of the following species -

Akebia quinata
Akebia trifoliata
Clematis armandii
Clematis montana
Cocculus orbiculatus
Cocculus thunbergii
Cocculus trilobus
Stephania tetrandra,

or an extract from such a plant, is prohibited.

Prohibition of sale, supply and importation of any medicinal product presented as consisting of or containing Mu Tong etc.

3. Subject to article 4 below, the sale, supply and importation of any medicinal product presented as consisting of or containing -

(a) *Mu Tong* or *Fangji*;

(b) a plant as referred to in article 2 above; or

(c) an extract from *Mu Tong*, *Fangji* or a plant as referred to in article 2 above,

is prohibited.

Exceptions to the prohibitions imposed by articles 2 and 3 above

⁴ OJ No. L1, 3.1.94, p.3.

⁵ OJ No. L1, 3.1.94, p.572.

⁶ “Plant” includes part of a plant; see section 132(1) of the Act.

4. – (1) The prohibitions imposed by articles 2 and 3 above shall not apply where a medicinal product as referred to in those articles is sold or supplied to, or, in the case of importation, is imported by or on behalf of, any of the following persons–

- (a) a food analyst or food examiner within the meaning of section 30 of the Food Safety Act 1990 (⁷);
- (b) a food analyst or food examiner within the meaning of Article 30 or 31 of the Food Safety (Northern Ireland) Order 1991 (⁸);
- (c) an authorised officer within the meaning of section 5(6) of the Food Safety Act 1990, or Article 2(2) of the Food Safety (Northern Ireland) Order 1991;
- (d) a person duly authorised by an enforcement authority under sections 111 and 112 of the Act;
- (e) a sampling officer within the meaning of Schedule 3 to the Act.

(2) The prohibitions on importation imposed by articles 2 and 3 above shall not apply where a medicinal product as referred to in those articles is imported–

- (a) from a member State of the European Community; or
- (b) where the product originates (⁹) in the European Economic Area, from an EEA State which is not also a member State of the European Community.

(3) The prohibitions imposed by articles 2 and 3 above shall not apply where a medicinal product as referred to in those articles is the subject of a product licence (¹⁰), a marketing authorization within the meaning of regulation 1(4)(a) of the Medicines for Human Use (Marketing Authorisations Etc.) Regulations 1994 (¹¹) or a certificate of registration within the meaning of regulation 1(2) of the Medicines (Homoeopathic Products for Human Use) Regulations 1994 (¹²).

Signed by authority of the Secretary of State for Health

⁷ 1990 c.16.

⁸ S.I. 1991/762 (N.I. 7); as amended by S.I. 1996/1633 (N.I. 12).

⁹ See Protocol 4 (on rules of origin) annexed to the EEA Agreement, as amended by the Decision of the EEA Joint Committee No. 6/94 amending Protocol 4 to the EEA Agreement (OJ No. L95, 14.4.94, p.22).

¹⁰ “Product licence” has the meaning assigned to it by section 7 of the Act.

¹¹ S.I. 1994/3144; as amended by S.I. 1998/3105 and 2000/ .

¹² S.I. 1994/105; as amended by S.I. 1994/899, 1995/541, 1996/482, 1998/3105 and 1996/566.

2000 Parliamentary Under Secretary of State
Department of Health

2000 Minister of Health,
Social Services and Public Safety

EXPLANATORY NOTE
(*This note is not part of the Order*)

This Order prohibits the sale, supply, and importation, of any medicinal product -

- (a) consisting of or containing a plant belonging to any of the following species - *Akebia quinata*, *Akebia trifoliata*, *Clematis armandii*, *Clematis montana*, *Cocculus orbiculatus*, *Cocculus thunbergii*, *Cocculus trilobus*, *Stephania tetrandra*, or an extract from such a plant; or
- (b) presented as consisting of or containing *Mu Tong* or *Fangji*, a plant as referred to in (a) above, or an extract from such a substance or plant.

These prohibitions are subject to the following exceptions-

- (i) where the sale or supply is to, or the importation is made by or on behalf of, a person exercising functions in relation to the enforcement of food or medicines legislation;
- (ii) in the case of the prohibitions on importation, where the product is imported from a member State of the European Community, or, where the product originates in the European Economic Area, from a State Party to the European Economic Area Agreement which is not also a member State;
- (iii) where the product is the subject of a product licence, marketing authorization or homoeopathic certificate of registration.

This Order was notified to the European Commission in accordance with European Parliament and Council Directive 98/34/EC, Article 8 (OJ No. L204, 21.7.1998, p.37) as amended by European Parliament and Council Directive 98/48/EC, Article 1(4) (OJ No. L217, 5.8.1998, p.18), and in accordance with Council Directive 75/319/EEC, Article 33 (OJ. No. L147, 9.6.1975, p.13).

This Order shall come into force on March 2000 and shall continue in force until the end of 30th June 2001, when it shall expire.

DRAFT REGULATORY IMPACT ASSESSMENT

The Medicines (Mu Tong etc.) (Temporary Prohibition) Order 2000

1. PURPOSE AND INTENDED EFFECT OF THE PROPOSAL

The Issue

A number of medicinal plants, which in themselves are considered harmless when correctly administered, are prone to being substituted by, or confused with, highly toxic plants of the genus *Aristolochia*. Following cases of serious illnesses associated with the mistaken use of *Aristolochia* species in herbal remedies, the import, sale and supply of unlicensed herbal remedies containing *Aristolochia* species was made illegal in July 1999. A subsequent sampling and analysis exercise, conducted by the Medicines Control Agency (MCA), showed that a significant proportion of herbal remedies believed to be at risk of containing aristolochic acids, did in fact do so. On the advice of the Committee on Safety of Medicines (CSM), the MCA is introducing a ban on unlicensed medicines containing, or presented as containing, a number of specified plants.

Objectives

The objective is to protect public health.

Risk Assessment

In 1999, two cases of serious kidney damage were reported in patients in the UK who had been prescribed unlicensed medicines which mistakenly contained a species of *Aristolochia*. There is also wider international evidence of similar incidents.

There are specific reasons why certain plants are at particular risk of confusion with *Aristolochia* species. One reason is the similarity of the shortened form of the common (or pin yin) names under which the ingredients of Chinese herbal remedies are traded. Also, in Chinese tradition, a number of herbal ingredients may be interchangeable with *Aristolochia* species.

The MCA has sampled and analysed products thought to be at particular risk of containing *Aristolochia* species. 44% of the samples tested contained aristolochic acids, an indicator of the presence of *Aristolochia* species.

2. OPTIONS

Identified options

Three main options have been identified:

Option 1 – continue to rely on the present control, namely that the import, sale or supply of unlicensed medicines containing *Aristolochia* species is not permitted

Option 2 – introduce an Order banning the import, sale or supply of unlicensed medicines containing specified plants at risk of confusion with *Aristolochia* species unless due diligence can be shown to have been taken in ensuring that *Aristolochia* species are not present in the unlicensed medicine

Option 3 – introduce an Order providing for an absolute prohibition on the import, sale or supply of unlicensed medicines containing, or presented as containing, specified plants at risk of confusion with *Aristolochia* species.

Issues of equity or fairness

In principle it is undesirable to place restrictions on the use of products which are not believed to be inherently harmful. However, the recent sampling and analysis exercise has clearly shown that public health is compromised by the availability of unlicensed medicinal products where there is a serious risk that toxic *Aristolochia* species are present. The results indicate that standards of manufacturing practice currently vary widely in the unlicensed TCM sector.

The proposed prohibition is being put in place on the understanding that it could be modified or withdrawn if and when satisfactory control systems are in place to ensure the safety and quality of TCM products. A subgroup of the CSM is to advise on the circumstances in which in future it might be feasible to withdraw or modify the prohibition.

3. BENEFITS IDENTIFIED AND QUANTIFIED

The proposed legislation will benefit the public by reducing the risk of exposure to toxic *Aristolochia* species leading to nephrotoxicity and carcinoma. Additional costs to the NHS incurred, for example, with dialysis treatment and transplantations, with other concomitant expenses, will also be avoided.

4. COMPLIANCE COSTS FOR BUSINESS

Business sector affected

Manufacturers of medicinal products come under business sector 24421 (Manufacture of medicaments) *Business Monitor PA1003 – Size analysis of United Kingdom Business (1996)*.

Recurring costs

The proposals may have some ongoing financial impact as businesses and practitioners will need to consider the use of alternative remedies and ingredients in place of those affected by the prohibition. It is not clear whether, and if so to what extent, available alternatives will be more expensive and/or the profitability of businesses will be affected.

However, given the limited regulatory controls which apply to the generality of unlicensed herbal remedies, the sector is particularly dependent on continuing public confidence that products are safe and of good quality. To maintain public confidence

it may not be sufficient for TCM businesses simply to switch to alternative ingredients unaffected by the prohibition. The problems which have arisen with *Aristolochia* species underline a wider need for businesses and practitioners dealing in unlicensed medicines to ensure that the ingredients are sourced from reputable suppliers and products are manufactured in properly controlled conditions. Responsible businesses will wish to ensure that medicinal products contain the advertised ingredients only, and in particular do not contain any dangerous or illegal ingredients.

Non-recurring costs

Importers and practitioners needing to dispose of any present stocks of unlicensed medicines affected by the new prohibition are likely to incur loss of income from sales foregone.

Total compliance costs

It is not possible to put a figure on the total compliance costs. However, it is likely that any *direct* costs incurred in complying with the proposed banning Order would be outweighed by *indirect* costs resulting from loss of business if no effective action were taken.

5. SUMMARY AND RECOMMENDATIONS

Option 1: the existing prohibition – although necessary - does not of itself adequately protect the public from the inadvertent inclusion of *Aristolochia* species in unlicensed medicines

Option 2: this option, of a conditional prohibition, would be preferable in principle if the appropriate safety and quality controls were in place. However, they are not, and with the sampling and analysis results clearly showing the variable quality of manufacturing practice in the TCM sector, the MCA accepts the CSM's advice that this option would not at present provide the public with sufficient protection

Option 3: on account of the serious risk to public health posed by the use of toxic *Aristolochia* species and the current lack of adequate controls to ensure that only safe ingredients are used, this is the preferred option

We therefore recommend Option 3: an Order prohibiting the import, sale or supply of unlicensed medicines consisting of or containing, or presented as consisting of or containing, specified plants at risk of confusion with *Aristolochia* species.

6. ENFORCEMENT, SANCTIONS, MONITORING AND REVIEW

The ban will be enforced by the MCA's Enforcement Unit as part of its existing compliance and enforcement responsibilities in protecting public health. Offenders will be liable to prosecution, and unlicensed medicines will be included in the Agency's regular product monitoring programme. The need for the ban will be reviewed as and when appropriate safety and quality controls are in place.

