Permitted indications under the Directive on Traditional Herbal Medicinal Products

1. Introduction

1.1 This note gives some initial guidance or pointers to industry as to the kind of indications that would be likely to be permitted, or not permitted, in products registered under the Directive on Traditional Herbal Medicinal Products. It responds to a request from the industry's Herbal Forum for guidance. In addition the MHRA has become aware through responses to its voluntary pre-application notification scheme that some parts of industry may not be fully familiar with the considerations that help to determine whether a product is suitable for use without medical supervision.

2. Requirements of the Directive

2.1 The Directive provides that products eligible for the registration scheme:

> *will have indications exclusively appropriate to traditional herbal medicinal products which, by virtue of their composition and purpose, are intended and designed for use without the supervision of a medical practitioner for diagnostic purposes or for prescription or monitoring of treatment.*

The Directive restricts the simplified registration procedure to products for oral or external use and/or inhalation.

2.2 Products registered must include a statement in their labelling, patient information leaflet and advertising that the product is a traditional herbal medicinal product for use in specified indication(s) exclusively based on long-standing use.

2.3 The MHRA anticipates that the great majority of successful registration applications will be for products with General Sale List status, although a small number may be restricted to Pharmacy sale.

2.4 Looking further ahead, in the event that statutory regulation is introduced for herbal practitioners the possibility could be explored of whether there are traditional herbal medicines that are suitable for use without medical supervision but nonetheless for safe usage would require the supervision by a registered herbalist.

3. Factors relevant to the need for medical supervision

3.1 Some medicines on account of their ingredient(s) may be inherently unsuitable for use without medical supervision, irrespective of the proposed indications.

3.2 A medicine may present a danger either directly or indirectly, even when taken correctly, if used without medical supervision. This could arise if the product causes adverse reactions that are important because of their seriousness, severity or frequency; or the adverse reaction is one for which there is no suitable preventative action such as the exclusion of a clearly identifiable risk group.

3.3 A requirement for medical supervision may be appropriate if there is evidence that an ingredient or product is widely misused or abused, leading to risk of harm.

3.4 There are other factors that need to be taken into account in determining whether a medicine with its associated indication(s) is suitable for use without medical supervision. Consideration needs to give to whether:

- symptomatic treatment might mask an underlying condition requiring medical attention;
- incorrect use might lead to a delay in seeking medical treatment with adverse consequences for the patient;
- where particular symptoms are outward manifestations of a diverse range of underlying pathologies and the patient cannot easily self-diagnose the cause of such symptoms it may be inappropriate to provide symptomatic treatment without management of the underlying disease;
- there is a possibility of serious asymptomatic damage in chronic conditions;
- the conditions or symptoms for which the product is indicated can be correctly diagnosed without medical supervision or easily recognised following initial medical diagnosis. The problem of excluding conditions with similar symptoms but unsuitable for treatment with the product in question may need to be addressed;
- patients understand the natural course of the disease and the possibility and consequences of reoccurrence; and can they recognise contraindications and understand essential precautions and warnings;
- a high incidence of conditions listed as contraindications, extensive precautions and warnings or a high rate of usage of interacting drugs in the population of patients likely to use the drug may increase the incidence and risk of misuse;
- there is significant danger to health if the patient uses the product when it is <u>not</u> indicated, exceeds the recommended dose or recommended length of treatment or fails to heed the contraindications or warnings. Consideration of the consequences of misuse is an important component of the overall safety profile of the product. Concerns over the risk of misuse are lessened where the product causes only few, non-serious side effects.

3.5 Each case, and especially where there is any doubt over the suitability of use without medical supervision, needs to be considered carefully in the round. It is also important to take full account of whether patient information might adequately mitigate any risks associated with use without medical supervision.

4. <u>Examples of indications likely to be permissible in a registered traditional herbal medicine.</u>

4.1 Attached at Annex 1 is a list of illustrative examples of indications likely to be permissible in products registered under the Directive. Clearly use in specific registered products would be dependent on evidence of traditional usage. The list shows conditions that would be suitable for self-medication and, depending on the herbal ingredients, would not normally require medical intervention. It should be stressed that this list has no formal or legal status in relation to this Directive and there are also likely to be other indications not listed that would also be suitable.

5. Examples of conditions unlikely to be permissible for a registered traditional herbal medicine

5.1 Attached at Annex 2 is a list giving pointers as to the kind of conditions for which it is unlikely that it would be possible to get product registrations because such uses would require medical intervention to ensure safe treatment. Again, this list of examples has no formal or legal status in relation to this Directive and there will be other conditions not included for which the same consideration applies.

6. Indications expressed in non-conventional terms

6.1 The question has been raised as to whether indications under the Directive may be expressed in terms that would not be familiar in western orthodox medicine. This issue might arise for example in relation to traditional Chinese or Ayurvedic medicine. Under the Directive the indication should be appropriate to the nature of the tradition. The MHRA would not therefore rule out proposed indications simply on the basis that the indications would not be used in conventional western medicine. However, the factors outlined at Section 3 above are also relevant to this situation. For example, if the public are not able to understand the indication there is the likelihood of misuse.

6.2 The Directive does provide some flexibility as to the wording of indications. Applicants are required to provide evidence of the traditional use of corresponding product(s). One of the features of corresponding product(s) is that they have the "*same or similar intended purpose*". Applicants may find this degree of flexibility helpful in seeking to express traditional indications from non-western herbal traditions in a way that is consistent with the tradition as well as understandable to an average member of the public buying the product on the UK market.

7. Suitability of registered herbal medicines for general sale.

7.1 Under the provisions of Part III of the Medicines Act 1968 General Sale List classification is appropriate for medicines which can, with reasonable safety, be sold or supplied otherwise than by or under the supervision of a pharmacist. When considering the suitability of a product for GSL status it is necessary to confirm firstly that the hazard to health and the risk of misuse is small and that significant special precautions in handling are not required. If there are no safety impediments it is then necessary to consider whether the convenience to the purchaser outweighs the benefit of availability of professional advice at the point of sale. As indicated above, the MHRA anticipates that the majority of registered products will be suitable for GSL status, with only a minority requiring restriction to pharmacy sale.

8. Conclusion

8.1 The MHRA will keep this guidance note under review and may extend it in the light of further experience in preparing for the launch of the traditional herbal medicines scheme. In addition, the MHRA is also aware of specific queries raised about suitable indications relating to several currently very popular herbal ingredients. The Agency is giving thought as to whether further guidance can usefully be given on these specific queries.

Annex 1

Examples of indications likely to be permitted in registered traditional herbal medicines

System or part of the body or disease	Permitted traditional use:
1. The cardio-vascular system.	**'symptomatic relief of':** Chilblains. Haemorrhoids by relief of symptoms by means of locally effective preparations or stool softening agents and lubricants.
2. The endocrine system.	Weight reduction dependent upon mechanism involving a reduced calorie or joule intake.
3. The gastro-intestinal system.	**'symptomatic relief of':** Indigestion, heart burn, hyperacidity, dyspepsia, halitosis (bad breath) or flatulence. Colicky pain, stomach ache or nausea. Occasional or non-persistent diarrhoea or constipation. Travel sickness or related symptoms.
4. The genito-urinary system and mammary glands.	**'symptomatic relief of':** Dysmenorrhea. Sore nipples during lactation by means of local applications.
5. Infections including viral, bacterial and fungal diseases.	**'symptomatic relief of':** 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 prevention of athlete's foot. Aphthous ulcers.

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

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

Annex 2

Examples of conditions for which indications are unlikely to be permitted in registered traditional herbal medicines

Bone diseases
Cardiovascular diseases
Chronic insomnia
Diabetes and other metabolic diseases
Diseases of the liver, biliary system and pancreas
Endocrine diseases
Genetic disorders
Joint, rheumatic and collagen diseases*
Malignant diseases
Psychiatric diseases
Serious disorders of the eye and ear
Serious gastrointestinal diseases
Serious infectious diseases including HIV-related diseases and tuberculosis
Serious neurological and muscular diseases**
Serious renal diseases
Serious respiratory diseases
Serious skin disorders
Sexually transmitted diseases

* except for the purpose of the treatment of the symptoms of sprains or strains or the relief of pain or stiffness of rheumatic or non-serious arthritic conditions

** except for the purpose of prevention of neural tube defects.