HERBAL MEDICINES: Product Licence To Traditional Herbal Registration in the UK

Presented by: Mariam Aslam

ESCOP

- **E**uropean **S**cientific **C**ooperative **O**n **P**hytotheapy (ESCOP)
- Founded in June 1989 as an umbrella organisation representing national phytotherapy associations across Europe, especially in their discussions with European medicines regulators.
- Delegates from each member country of ESCOP as well as others as appropriate.
- Issue harmonised European Monographs on the Medicinal Uses of Plant Drugs on the basis of published information and taking account of the traditional use within European member states.
- Website www.escop.com

Introduction

- Legal Definition of Herbal Medicine
- The Medicines Act 1968
- Review of Product License of Right in the UK
- European Traditional Herbal Medicinal Products Directive (THMPD) 2004/24/EC
- Key Challenges for THR Holders

Legal Definition of Herbal Medicine

In accordance with Article 1 of EU Directive 2001/83/EC, relating to medicinal products for human use, as amended:

***Herbal medicinal product**:*

Any **medicinal product**, exclusively containing as active ingredients one or more **herbal substances** or one or more **herbal preparations**, or one or more such herbal substances in combination with one or more such herbal preparations.

Legal Definition of Herbal Medicine

In accordance with Article 1 of EU Directive 2001/83/EC, relating to medicinal products for human use, as amended:

***Medicinal product**:*

(a) Any substance or combination of substances presented as having **properties for treating or preventing disease in human beings**; or

(b) Any substance or combination of substances which may be **used in or administered to human beings either with a view to restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action,** or to making a medical diagnosis.

Legal Definition of Herbal Medicine

In accordance with Article 1 of EU Directive 2001/83/EC, relating to medicinal products for human use, as amended:

***Herbal substances**:*

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

Legal Definition of Herbal Medicine

In accordance with Article 1 of EU Directive 2001/83/EC, relating to medicinal products for human use, as amended:

***Herbal preparations**:*

Preparations obtained by subjecting herbal substances to treatments such as extraction, distillation, expression, fractionation, purification, concentration or fermentation. These include comminuted or powdered herbal substances, tinctures, extracts, essential oils, expressed juices and processed exudates.

The Medicines Act 1968

What is the Medicines Act 1968 and why was it introduced:

- A legislation laid down by the UK government for the control of medicines for human use and veterinary use, including the manufacture and supply of medicines in the UK.

- Introduced in 1971 as a result of the Thalidomide tragedy.

The Medicines Act 1968

- *Herbal medicines under the Act:*

➢ When the Act came in to force, Product Licence of Right (PLR) were granted to existing herbal medicines already on the market.

➢ New herbal medicines then placed on the market making a medicinal claim on the label required a Product Licence (PL).

The Medicines Act 1968

- *Herbal medicines under the Act:*

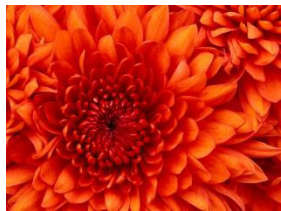
➢ Section 12(2) of the Act permitted exemption from regulation for “unlicensed herbal remedies” if it contained only one or more herbal substances, had a name which specified only the herb(s) and process, i.e. no trade name, and no medicinal claims were made for the product.

The Medicines Act 1968

- *Current status of the Act:*

➢ Since The Medicines Act 1968 there have been a number of amendments of the legislation on medicines for human use in the UK.

➢ The UK Medicines and Healthcare products Regulatory Agency (MHRA) initiated a project to consolidate and review UK medicines legislation. The result was The Human Medicines Regulations 2012 which came in to force in August 2012 and replaced much of the Act.



Review of Product Licence of Right (PLR) in the UK

- In 1975, a new European Community (EC) Directive highlighted that all PLRs, including herbal medicines, should be reviewed by May 1990.

- In 1988, the MHRA began their review of these herbal medicines and completed the task in the mid-1990.

Review of Product Licence of Right (PLR) in the UK

- During the review, the quality and safety of PLRs for herbal medicines were considered for continuation of their supply to the public.

- The PLRs that were accepted during the review, were granted a full Marketing Authorisation (MA) also referred to as Product Licence (PL).

European Traditional Herbal Medicinal Products Directive (THMPD) 2004/24/EC

- In 2004, a simplified procedure was introduced by Directive 2004/24/EC to enable EU Member States in implementing harmonised pharmaceutical legislation to traditional herbal medicinal products.

- European THMPD came into effect on 30 April 2011. Directive 2004/24/EC amends Directive 2001/83/EC for regulating traditional herbal medicinal products.

European Traditional Herbal Medicinal Products Directive (THMPD) 2004/24/EC

- The Directive established a regulatory approval process for herbal medicines in the European Union (EU) requiring each Member State to set up traditional herbal registration scheme for manufactured traditional herbal medicines that were suitable for use without medical supervision.

European Traditional Herbal Medicinal Products Directive (THMPD) 2004/24/EC

- Companies were no longer permitted to sell manufactured unlicensed herbal medicines unless they had an appropriate PL; either as a full MA based on the safety, quality and efficacy of the product or a Traditional Herbal Registration (THR) based on the safety, quality and evidence of traditional use of the product throughout a period of 30 years of which at least 15 years must have been within the European Union.

European Traditional Herbal Medicinal Products Directive (THMPD) 2004/24/EC

- THMPD was adopted in acknowledgment of the fact that companies could not provide evidence, in particular, for efficacy to meet the full requirements of a MA.

- The MHRA permitted companies to make transfer of PLs with traditional indications to traditional herbal registration (THR) status.

- Companies submitted, to the MHRA, simplified THR applications with updated Module 1 of the Common Technical Document (CTD) dossier including Summary of Product Characteristics (SPC), labelling & leaflet.

European Traditional Herbal Medicinal Products Directive (THMPD) 2004/24/EC

- Flexibility within Directive 2004/24/EC permitted companies to make amendments to the product as part of the process of transfer to THR.
- Examples of amendments included:

- clarifying indications in a way that is more meaningful to the consumer
- simplifying the product formulation and the quality controls, for example by removing non essential ingredients.

European Traditional Herbal Medicinal Products Directive (THMPD) 2004/24/EC

- In the UK, all transfers were completed in 2013.

- The MHRA granted the THR transfer on the conditions:
- ✓ At first renewal (5 years from date of grant), a full CTD Module 3 must be submitted to avoid cancellation of the THR.
- ✓ Genotoxicty data made available at renewal date.

- Since 2006, more than 300 THRs have been granted in the UK by the MHRA. Of these 300, more than 30 have been transfers.

Key Challenges for THR Holders

Prior to transfer, many companies did the minimum testing on their herbal products and had incomplete quality dossiers.

To ensure compliance with regulations and therefore remain legal, herbal medicines companies are currently experiencing many challenges, particularly for their first renewal commitments.

Key Challenges for THR Holders

- THR transfer renewal commitments:

Challenge:-

- Obtaining data for Good Agricultural and Collection Practice for Starting Materials of Herbal Origin (GACP) – geographical source and the conditions under which the herbal substance is obtained to ensure material of consistent quality.

Key Challenges for THR Holders

- ➢ THR transfer renewal commitments:

Challenges:-

- Analytical Research & Development for the requirement of specifications, test methods/validation for herbal substance, herbal preparation, herbal product
- ✓ Control of active ingredients – identifying and quantifying chemical markers (active and analytical).
- ✓ The control tests on the finished product - qualitative and quantitative determination of the active substance(s) is not possible due to combination of herbal substances or preparations masking each other.

Key Challenges for THR Holders

- THR transfer renewal commitments:

Challenge:-

- Stability testing -not possible to determine the stability of each active substance in herbal medicinal product containing combinations of several herbal substances or herbal preparations. The stability of the medicinal product should be determined by appropriate fingerprint chromatograms, appropriate overall methods of assay and physical tests.

Conclusion/Summary

Phase 1.
Medicines Act 1968

Phase 2.
Review of PLR

Phase 3.
EU THMPD

Phase 4.
Transfer of PL to THR

Phase 5.
Module 3 Dossier -THR renewal

Thank you