# Herbal Medicine:
## Two sides of the coin

by Everaldo Attard

Introduction
A Herbal Medicinal Product (HMP) may be classified either as a herbal with a Well-Established Use/s (WEU) or a Traditional Herbal Medicinal Product (THMP). Its status primarily depends on the toxico-pharmacological profile and the way the product is presented on the market.

Although scientific research on quality, safety and efficacy may be essentially the same for both categories, the manufacturer may present the HMP in either category as long as the product conforms to one of the two main Council Directives.1,2 The main differences between these two categories are outlined in table 1.

| | THMPs | Herbals with WEU |
|---|---|---|
| Discovery of product | Long History of Usage (30 years) | Discovered recently or use proven recently (10 years) |
| Proof of Efficacy | No proof. Bibliographic traditional information | Proof of efficacy by bibliographic clinical data |
| Proof of Safety | *In vitro* testing for genotoxicity and support by bibliographic data | *In vitro* and *in vivo* testing of product |
| Proof of Quality | Processed under pharmaceutical manufacturing procedures or as stated by an official European or Community Monograph | Processed under pharmaceutical manufacturing procedures. Reference to a Community Monograph can be made |
| Registration | Simplified Registration (registered HMPs) | WEU Marketing Authorisation (licensed HMPs) |
| Regulated by Council Directive | 2004/24/EC[1] | 2001/83/EC[2] |

**Table1**: The main differences and similarities for THMPs and herbals with WEU.

Proof of efficacy for HMPs
If the product efficacy has been proven scientifically, the HMP is probably a herbal with WEU. Scientific proof should be well-founded with appropriate in vitro and in vivo clinical trials, and with the relevant statistical backing. If no scientific efficacy is proven, the product may be a THMP. However, to qualify under this category the medicinal product should cover a traditional use for more than 30 years, with at least 15 years within the European Union. If this is fulfilled the product may proceed along the THMP line. Otherwise, additional information is required for the product to reach the market, either as a THMP with more bibliographical data, or as a herbal with WEU with more clinical data.

Routes of administration for HMPs
The route of administration has also an important implication on the categorisation of a HMP. A THMP should be administered orally, topically or by inhalation. In the case of herbals with WEU, these can be administered through any route of administration. This is because THMPs, intended to control or treat minor medical conditions, may be presented as over-the-counter (OTC) products for self treatment, while herbals with WEU are usually intended to control or treat more serious medical conditions and therefore require medical supervision. The latter are the prescription-only medicines (POM).

Doses and dosage regimens for HMPs
In spite of their medical intent, HMPs should contain specific herbal preparations or herbal substances with a specific dose range and frequency of administration. This is mandatory as a guide to the general public and healthcare professionals such as physicians and pharmacists. If the doses and dosing regimen are not included within the package leaflet (PL) and the HMP packaging, the product will fail to reach the market. Since these HMPs are usually extracts, the extracts are adjusted according to a valuable reference substance. These substances may be active markers, i.e. compounds that exhibit the pharmacological activity stated, or analytical markers, i.e. compounds that indicate the strong presence of a class of compounds but do not necessarily contribute to the pharmacological activity. These categorise HMPs into standardised and quantified extracts, respectively. However, there are other HMPs that cannot be standardised or quantified, and in most cases, such extracts are not granted a marketing authorisation. Further classification of HMPs within these categories, is beyond the scope of this article.

Additional active constituents to HMPs
If there are no additional active constituents then the product is likely to be classified as either a THMP or a herbal with a WEU. However, additional active constituents that are allowed in herbal preparations are vitamins and minerals. If these do not have a pharmacological role, vitamins and minerals may be omitted from the herbal medicinal product. On the other hand, if these are retained in the product, the quantities should be according to or less than the daily maximum requirements, depending on the frequency of daily administration.3 If there are other active constituents other than vitamins and minerals, the product may be either modified to eliminate these constituents, particularly if the constituents are toxic, or else considered as a herbal combination product. Combination products that are not supported by a traditional use may only be considered as herbals with WEU as long as there is bibliographic proof of clinical efficacy.4

Conclusion
The distinctive characteristics of HMPs guide healthcare professionals towards rational use of plant-derived natural products. This facilitates the integration of green medicine, with an optimum quality-safety profile, within modern prescribing and dispensing practices.

References
1. Directive 2004/24/EC of the European Parliament and of the Council of 31 March 2004 amending, as regards traditional herbal medicinal products, Directive 2001/83/EC on the Community code relating to medicinal products for human use. Official Journal L 136; 85-90. 2. Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use, Official Journal L 311; 67-128. 3. Legal Notice 239 of 2003. FOOD SAFETY ACT, 2002. Food Supplements Regulations, 2003. 22p.
4. Decision tree for the classification of traditional herbal medicinal products and herbal medicines with a well-established use at http://staff.um.edu.mt/eattl/THMPs/