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Reflection paper on quality of essential oils as active substances in herbal medicinal products/traditional herbal medicinal products

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1. Introduction

This reflection paper applies to essential oils used as active substances in herbal medicinal products (HMPs) both for human and veterinary use and in traditional herbal medicinal products (THMPs) for human use.

The purpose of this reflection paper is to consider aspects related to the nature and the specific production processes of essential oils.

The Directive 2001/83/EC as amended provides definitions for HMPs, herbal substances and herbal preparations. The same basic legislation applies to both HMPs and other medicinal products. An additional simplified registration procedure has been established for THMPs.

According to these definitions essential oils are herbal preparations.

The requirements for essential oils are not fully addressed in the existing quality guidelines.

The existing HMPC quality guidelines do not take account of the definitions of the Pharmacopoeia Europea (Ph. Eur.) monograph “Essential oils”.

The manufacturing processes for herbal preparations should be in line with the GMP Rules Part II.

The aim is to provide further guidance for manufacturers of essential oils and applicants on the documentation to be presented to the competent authorities.

Essential oils used as excipients are not considered in this reflection paper.

2. Discussion

Essential oils are widely used as fragrances and flavourings in the cosmetic and food sectors. Usage within the pharmaceutical sector, represents, in many cases, only a limited proportion of the commercial market. For these reasons essential oils present a number of particular issues similar to those of atypical substances from a regulatory standpoint when they are used as active pharmaceutical ingredients (APIs) in HMPs.

The production of essential oils is often performed by farmers or small companies with limited experience in the manufacturing of APIs for pharmaceutical use.

The starting materials used in the production of essential oils are normally fresh herbal substances.

The quality of a medicinal product is independent of its use and therefore all general principles of quality and quality guidance documents also apply to HMPs and THMPs.

Due to their complex nature, specific herbal guidelines provide further information on how the quality issues should be addressed in the case of herbal substances/herbal preparations/HMPs.

As a general principle, all manufacturers of the herbal preparation should be listed in the quality documentation. Where the essential oil is manufactured by farmers or very small companies this can present difficulties. In addition, it is often difficult to obtain sufficient information about the starting plant material used to produce the oil.

Normally a comprehensive specification for each herbal substance must be submitted. In the quality guidelines it is stated that in the case of essential oils used as APIs of HMPs, a specification for the herbal substance is required, unless fully justified. If fresh material is used and/or the oil production is linked to the collecting or harvesting processes, it is often difficult to establish a full analytical characterisation of the herbal substance. The identity of the herbal substance should be guaranteed,

but other tests (according to the Ph. Eur. monograph Herbal drugs) can be transferred to the essential oil.

For each herbal preparation, a comprehensive specification is required. It is known for essential oils that the risk for some contaminants, e.g. microbial contamination, is very low and in such instances absence of tests or reduced testing may be justified. In general, all sub-batches that are used for blending should comply with the specifications prior to mixing. However, it would appear that some Pharmacopoeia specifications are based on blended and reprocessed samples. Purification steps or reprocessing of essential oils are common procedures. The Ph. Eur. monograph refers to deterpenated, desesquiterpenated, rectified and 'x'-free essential oils. The Ph. Eur. monograph "mint oil, partly dementholised" is an example of such a modified essential oil. In the case of the Ph. Eur. monographs for eucalyptus oil and turpentine oil *Pinus pinaster* type, rectification of the oil is mentioned in the definition section of the monographs.

3. Conclusion

Essential oils used as APIs in HMPs are important commodities which raise a number of issues from a regulatory standpoint. Current guidance does not address fully the particular aspects of essential oils and further guidance is needed for manufacturers of essential oils and applicants on the documentation to be presented to the competent authorities.

The Interested Parties have provided examples and comments covering the range of different manufacturing processes which are specific for essential oils. Important points raised were the feasibility of a GMP compliant manufacturing process of the active substance and the practicability of GACP-regulations for the herbal substance. The quality of water used for the distillation of oil from fresh plant material performed in the fields was another point of discussion. The blending of sub-batches and the compliance of such sub-batches with the Ph. Eur. monograph was considered to be important. It was agreed that these data are used as basis for guidance in form of questions and answers. Questions and answers covering these issues have been included in the Questions & answers on quality of herbal medicinal products/traditional herbal medicinal products (EMA/HMPC/41500/2010). New questions and answers can be added if necessary.

4. References

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