

**MEDICINES AND HEALTHCARE PRODUCTS
REGULATORY AGENCY**

**UK HOMOEOPATHIC REGISTRATION SCHEME
GUIDANCE NOTES**

**THE MANUFACTURE AND CONTROL OF DOSAGE
FORMS FOR HOMOEOPATHIC PRODUCTS**

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THE MANUFACTURE AND CONTROL OF DOSAGE FORMS FOR HOMOEOPATHIC PRODUCTS

Introduction

Applications to register homoeopathic medicinal products should be accompanied by supporting data on the production and control of the dosage form. Since the Homoeopathic Directive (92/73/EEC) applies the provisions of the Pharmaceutical Directives, (65/65/EEC and 75/319/EEC et seq), the quality standards applied to homoeopathic medicines are similar to those applied to all other medicinal products. The special nature of homoeopathic products is such that where manufacturing processes for dosage forms are standardised, the supporting data can be held in a master file on the formulation to which the applicant may cross-refer. Due to the extremely low levels of stock present in the dosage form, it is particularly important to ensure that adequate planning and in-process control is applied to the manufacturing process in order to ensure batch-to-batch homogeneity. These guidelines outline the general requirements for the accompanying data, taking account of the variety of homoeopathic dosage forms which are registrable.

1. FORMULATION MASTER FILES

Applicants may choose to present data on 'inert' or 'un-medicated' dosage forms in the form of a formulation master file to which they may cross-refer following its approval.

The formulation master file should contain the following information:

- a) Formulation details
- b) Development pharmaceuticals
- c) Container to be used for marketing
- d) Method of manufacture, in-process controls, including application of the diluted stock
- e) Specification of inert or un-medicated dosage form
- f) Batch data of inert or un-medicated dosage forms
- g) Stability of inert or un-medicated dosage forms.

2. FORMULATION

Complete composition

Full details of the formulations should be provided including the theoretical composition of excipients in the final formulation.

Development pharmaceuticals

Details should be provided of any development work which is relevant to the formulation such as preservative efficacy data for topical creams, oral liquids and eye drops.

The role of the excipients should be described.

Container

A description of the container and closure should be provided, including specifications.

3. MANUFACTURE

Applicants should refer to the method set out in a named homoeopathic pharmacopoeia and should provide supplementary information as set out below. Applicants will be expected to comply with GMP requirements and take account of any special requirements for the production of homoeopathic products as set out in the Annex to the Orange Guide to GMP.

Batch size and manufacturing formula

Details of a typical batch size should be provided.

The quantity of stock to be added to the dosage form and the degree of dilution of the stock prior to it being added should be declared.

The manufacturing process

The key elements of the manufacturing process and any standard operating procedures used should be summarised.

Details should be provided of all measures taken to avoid cross contamination.

Any sterilisation procedures should be described.

In-process controls

Where in-process controls are used, these should be stated, for example during the dilution process.

Process validation

Information on process validation should be made available, particularly with regard to more sophisticated dosage forms. For sterile products (eye drops) and accepted pharmacopoeial method should be used.

Specifications

Specifications of excipients to be used in the un-medicated dosage form should be declared. Container specifications should be listed.

4. FINISHED PRODUCT SPECIFICATION

The finished product specification should control the organoleptic and physical characteristics of the product. An identity test should be included for the stock at low dilutions.

The finished product specification should take account of any special characteristics of the dosage form. For example, creams should include a control for preservatives, eye drops should be sterile.

Analytical controls

All methods used should be pharmacopoeial (BP or PhEur). Where a method is not appropriate, a suitable, validated alternative should be used.

Batch data

Batch data should be made available for at least three batches which should preferably be production batches.

5. DILUTION AND POTENTISATION

Details of the homoeopathic method used for dilution and potentisation should be provided, together with the method used to incorporate the diluted stock into the inert dosage form. Validation data should be provided to demonstrate that this process is uniform.

The quality and quantity of diluent should be described and details of any in-process controls provided.

6. STABILITY STUDIES

Stability studies should be carried out in the container for marketing and should be conducted at a defined temperature or range of temperatures. The extent to which stability studies are carried out will require careful consideration and will depend upon the nature of the product. Examples of what might be required include preservative efficacy data for creams, or maintenance of alcohol content for oral liquids.

The stability of tablets or granules medicated using high dilutions of stock can be established and the results extrapolated to other tablets, provided an identical container and manufacturing process are used.

For more complex dosage forms such as creams or multidose eye drops, stability should be evaluated for individual products.

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