

**MEDICINES AND HEALTHCARE PRODUCTS REGULATORY
AGENCY**

**GUIDANCE NOTES FOR THE SIMPLIFIED HOMEOPATHIC
REGISTRATION SCHEME & UK HOMEOPATHIC
NATIONAL RULES SCHEME THE MANUFACTURE AND
CONTROL OF DOSAGE FORMS FOR HOMEOPATHIC PRODUCTS**

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THE MANUFACTURE AND CONTROL OF DOSAGE FORMS FOR HOMEOPATHIC PRODUCTS

Introduction

Applications to register homeopathic medicinal products should be accompanied by supporting data on the production and control of the dosage form. The quality standards applied to homeopathic medicines are similar to those applied to all other medicinal products. The special nature of homeopathic 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. In case of 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 homeopathic 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.

Pharmaceutical development

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 and justified.

Container

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

3. MANUFACTURE

Applicants marketing a homeopathic medicinal product in the whole of the UK or Northern Ireland only should refer to a method set out in the European Pharmacopoeia, or in the absence of a description there, the British Pharmacopoeia or a pharmacopoeia used officially in an EEA State.

Applicants marketing a homeopathic medicinal product in Great Britain only should refer to a method set out in the European Pharmacopoeia, or in the absence of a description there, the British Pharmacopoeia or a pharmacopoeia used officially in a country that is included in a list published by the MHRA.

The MHRA list can be found at this link [<https://www.gov.uk/guidance/register-a-homeopathic-medicine-or-remedy>]

Confirmation of compliance with a named pharmacopoeia should be provided with 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 homeopathic products. .

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

For products marketed in the whole of the UK or Northern Ireland only, all methods used should be pharmacopoeial (Ph. Eur, BP or a pharmacopoeia used officially in an EEA State).

For products marketed in Great Britain only, all methods used should be pharmacopoeial (Ph. Eur, BP or a pharmacopoeia included in a list published by the MHRA).

The MHRA list can be found at this link [<https://www.gov.uk/guidance/register-a-homeopathic-medicine-or-remedy>]

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 homeopathic 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 and reproducible. 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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