INTERNATIONAL PHARMACOPOEIA

MONOGRAPH ON ORAL POWDERS

DRAFT FOR COMMENT

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INTERNATIONAL PHARMACOPOEIA MONOGRAPH ON
ORAL POWDERS

**DRAFT FOR COMMENT**

**Timetable**

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<tr>
<td>Need for monograph identified at a Consultation</td>
<td>July 2005</td>
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<tr>
<td>Preliminary draft monograph prepared using the <em>Ph. Int.</em> approach for general monographs for dosage forms and taking account of the general monographs published in the <em>Ph. Eur.</em> and <em>BP</em></td>
<td>September 2005</td>
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<tr>
<td>Preliminary draft monograph mailed to July 2005 Consultation participants for comment, and advice sought from Professor Henning Kristensen</td>
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<tr>
<td>Presentation to 40th Expert Committee on Specifications for Pharmaceutical Preparations for discussion/adoption</td>
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ORAL POWDERS: Draft proposal for the International Pharmacopoeia (October 2005)

The requirements of this monograph do not necessarily apply to powders to be used for the preparation of oral solutions or suspensions.

Definition. Oral powders are preparations consisting of solid, loose, dry particles of varying degrees of fineness. They contain one or more active ingredients, with or without excipients and, if necessary, authorized colouring matter and flavouring substances. They are generally administered in or with water or another suitable liquid. They may also be swallowed directly. They are presented as single-dose or multidose preparations.

Multidose oral powders require the provision of a measuring device capable of delivering the quantity prescribed. Each dose of a single-dose powder is enclosed in an individual container, for example a sachet or a vial.

Manufacture. The manufacturing process for oral powders should meet the requirements of Good Manufacturing Practice, especially with regard to cross contamination.

In the manufacture of oral powders, means are taken to ensure a suitable particle size with regard to the intended use

In the manufacture, packaging, storage and distribution of oral powders, suitable means are taken to ensure their microbial quality.

The following information is intended to provide very broad guidelines concerning the main steps to be followed during production, indicating those that are the most important.

Appropriate measures should be taken to counteract segregation of the components of the powder mixture. Segregation takes place whenever a free-flowing powder consisting of particles of a range of sizes is handled, including the mixing stage and emptying of the mixer container. The prime means to counteract segregation is to use components of approximately the same particle size. Because of the risk of segregation, oral powders containing a low proportion of the active ingredient, say less than 5 % of total mass, should preferably be prepared as single-dose preparations.

The intended mass of one dose of an oral powder should be at least 500 mg to minimize the effect of loss of powder when taken from a single-dose container or to allow a proper dosing when using a measuring device.
In the production of oral powders, the components of the powder mixture are passed individually through a sieve to remove lumps and particle aggregates. The weighed masses of the sieved components, preferably of a uniform particle size, are then transferred to a mixer suitable for mixing free-flowing powders. The greatest risk of segregation of the powder mixture occurs when emptying the mixer container and when the powder mixture is dosed into single-dose containers or multidose containers. The suitability of the mixing equipment and the dosing devices is documented by a validation procedure.

Throughout manufacturing, certain procedures should be validated and monitored by carrying out appropriate in-process controls. These should be designed to guarantee the effectiveness of each stage of production. In-process controls during the manufacture of oral powders should include the dosing by mass of the powder in the containers.

[Note from the Secretariat: This section of the monograph has been completed based on advice from Professor Kristensen. He noted that: Generally, oral powders should be used only for ‘high dose’ preparations (analgesics, etc.). I think, however, it is necessary to recommend that ‘low dose’ preparations are provided in single-dose containers. Further, I suggest a minimum weight of the dose; 500 mg was the minimum we used in the old Nordic Pharmacopoeia. Regarding in-process controls: Mixing and dosing must be validated to ensure that the process can provided the intended quality. When validated, I think that an in-process control of the mass uniformity suffices.]

Visual inspection. Inspect the powder, using at least [20] containers for single-dose preparations. Evidence of physical and/or chemical instability is demonstrated by noticeable changes in physical appearance, including texture [e.g. clumping] or colour.

Uniformity of content. See the general requirements 5.1 Uniformity of content of single-dose preparations. Single-dose oral powders with a content of active ingredient of less than 5 mg or less than 5 per cent of the total mass comply with the test , unless otherwise specified in the individual monograph. If the preparation has more than one active ingredient, the requirement applies only to those active ingredients that fall into the above category.

[Note from the Secretariat: it is proposed to apply the limits as for capsules and suppositories.]

Uniformity of mass. See the general requirements 5. 2 Uniformity of mass of single-dose preparations. Single-dose oral powders comply with the test. If the test for uniformity of content is prescribed for all active ingredients, the test for uniformity of mass is not required.

[Note from the Secretariat: it is proposed to apply the limits as for capsules.]

Uniformity of mass of doses taken from multidose containers. Weigh individually 20 doses taken at random from one or more multidose containers with the measuring device provided and determine the individual and average masses. Not more than two of the individual masses deviate by more than 10 % from the average mass and none deviates by more than 20 %.

[Note from the Secretariat: Inclusion of the above test is recommended by Professor Kristensen who indicated that it was introduced into the Ph. Eur. because OMCL’s showed very bad compliance of measuring devices on the European market.]
Labelling

Every pharmaceutical preparation must comply with the labelling requirements established under Good Manufacturing Practice.

The label on the immediate container should include:

(1) the name of the pharmaceutical product;
(2) the name(s) of the active ingredients; INNs should be used wherever possible;
(3) for single-dose preparations, the amount of the active ingredient(s) per container and for multidose preparations, the amount of active ingredient in a suitable quantity by weight;
(4) the batch (lot) number assigned by the manufacturer;
(5) the expiry date and, when required, the date of manufacture;
(6) any special storage conditions or handling precautions that may be necessary;
(7) directions for use, warnings, and precautions that may be necessary;
(8) the name and address of the manufacturer or the person responsible for placing the product on the market.

Storage. If the preparation contains volatile ingredients, the oral powder should be kept in a tightly closed container.

Requirements for specific types of oral powder

Effervescent powders

Definition. Effervescent powders are presented as single-dose or multidose preparations and generally contain acid substances and carbonates or hydrogen carbonates which react rapidly in the presence of water to release carbon dioxide. They are intended to be dissolved or dispersed in water before administration.

Storage. Effervescent powders should be kept in tightly closed containers.

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