micro-organisms; recommendations on this aspect are provided in the text on Methods of preparation of sterile products (5.1.1).

In the manufacture of ear preparations containing dispersed particles, measures are taken to ensure a suitable and controlled particle size with regard to the intended use.

TESTS

Uniformity of content (2.9.6). Unless otherwise prescribed or justified and authorised, single-dose ear preparations with a content of active substance less than 2 mg or less than 2 per cent of the total mass comply with test B for uniformity of content of single-dose preparations. If the preparation has more than one active substance, the requirement applies only to those ingredients that correspond to the above conditions.

Uniformity of mass (2.9.5). Single-dose ear preparations comply with the test for uniformity of mass of single-dose preparations. If the test for uniformity of content is prescribed for all the active substances, the test for uniformity of mass is not required.

Sterility (2.6.1). Where the label indicates that the ear preparation is sterile, it complies with the test for sterility.

STORAGE

If the preparation is sterile, store in a sterile, airtight, tamper-proof container.

LABELLING

The label states:

– the name of any added antimicrobial preservative,
– where applicable, that the preparation is sterile,
– for multidose containers, the period after opening the container after which the contents must not be used. This period does not exceed 4 weeks, unless otherwise justified and authorised.

Ear-drops and sprays

DEFINITION

Ear-drops and sprays are solutions, emulsions or suspensions of one or more active substances in liquids suitable for application to the auditory meatus without exerting harmful pressure on the ear-drum (for example, water, glycols or fatty oils). They may also be placed in the auditory meatus by means of a tampon impregnated with the liquid. Emulsions may show evidence of phase separation but are readily redispersible on shaking. Suspensions may show a sediment which is readily dispersed on shaking to give a suspension which remains sufficiently stable to enable the correct dose to be delivered.

Ear drops are usually supplied in multidose containers of glass or suitable plastic material that are fitted with an integral dropper or with a screw cap of suitable materials incorporating a dropper and rubber or plastic teat. Alternatively, such a cap assembly is supplied separately. Sprays are usually supplied in multi-dose containers fitted with an appropriate applicator. When sprays are supplied in pressurised containers, these comply with the requirements of the monograph on Pressurised pharmaceutical preparations (0523).

Semi-solid ear preparations

DEFINITION

Semi-solid ear preparations are intended for application to the external auditory meatus, if necessary by means of a tampon impregnated with the preparation.

Semi-solid ear preparations comply with the requirements of the monograph on Semi-solid preparations for cutaneous application (0132).

They are supplied in containers fitted with a suitable applicator.

Ear powders

DEFINITION

Ear powders comply with the requirements of the monograph on Powders for cutaneous application (1166).

They are supplied in containers fitted with a suitable device for application or insufflation.

Ear washes

DEFINITION

Ear washes are preparations intended to cleanse the external auditory meatus. They are usually aqueous solutions with a pH within physiological limits.

Ear washes intended for application to injured parts or prior to a surgical operation are sterile.

TESTS

Deliverable mass or volume (2.9.28). Ear washes supplied in single-dose containers comply with the test.

Ear tampons

DEFINITION

Ear tampons are intended to be inserted into the external auditory meatus. They comply with the requirements of the monograph on Medicated tampons (1155).

EYE PREPARATIONS

Ophthalmica

DEFINITION

Eye preparations are sterile liquid, semi-solid or solid preparations intended for administration upon the eyeball and/or to the conjunctiva or for insertion in the conjunctival sac.

Where applicable, containers for eye preparations comply with the requirements of Materials used for the manufacture of containers (3.1 and subsections) and Containers (3.2 and subsections).

Several categories of eye preparations may be distinguished:

– eye drops,
– eye lotions,
– powders for eye drops and eye lotions,
– semi-solid eye preparations,
– ophthalmic inserts.

PRODUCTION

During the development of an eye preparation, the formulation for which contains an antimicrobial preservative, the effectiveness of the chosen preservative shall be demonstrated to the satisfaction of the competent authority.

A suitable test method together with criteria for judging the preservative properties of the formulation are provided in the text on Efficacy of antimicrobial preservation (5.1.3).
Eye preparations are prepared using materials and methods designed to ensure sterility and to avoid the introduction of contaminants and the growth of micro-organisms; recommendations on this aspect are provided in the text on Methods of preparation of sterile products (5.1.1).

In the manufacture of eye preparations containing dispersed particles, measures are taken to ensure a suitable and controlled particle size with regard to the intended use.

TESTS

Sterility (2.6.1). Eye preparations comply with the test for sterility. Applicators supplied separately also comply with the test for sterility. Remove the applicator with aseptic precautions from its package and transfer it to a tube of culture medium so that it is completely immersed. Incubate and interpret the results as described in the test for sterility.

Deliverable mass or volume (2.9.28). Liquid and semi-solid eye preparations supplied in single-dose containers comply with the test.

STORAGE

Unless otherwise prescribed, store in a sterile, airtight, tamper-proof container.

LABELLING

The label states the name of any added antimicrobial preservative.

Eye-drops

DEFINITION

Eye-drops are sterile aqueous or oily solutions or suspensions of one or more active substances intended for instillation into the eye.

Eye-drops may contain excipients, for example, to adjust the tonicity or the viscosity of the preparation, to adjust or stabilise the pH, to increase the solubility of the active substance, or to stabilise the preparation. These substances do not adversely affect the intended medicinal action or, at the concentrations used, cause undue local irritation.

Aqueous preparations supplied in multidose containers contain a suitable antimicrobial preservative in appropriate concentration except when the preparation itself has adequate antimicrobial properties. The antimicrobial preservative chosen must be compatible with the other ingredients of the preparation and must remain effective throughout the period of time during which eye-drops are in use.

If eye-drops are prescribed without antimicrobial preservatives they are supplied wherever possible in single-dose containers. Eye-drops intended for use in surgical procedures do not contain antimicrobial preservatives and are supplied in single-dose containers.

Eye-drops that are solutions, examined under suitable conditions of visibility, are practically clear and practically free from particles.

Eye-drops that are suspensions may show a sediment that is readily redispersed on shaking to give a suspension which remains sufficiently stable to enable the correct dose to be delivered.

Multidose preparations are supplied in containers that allow successive drops of the preparation to be administered. The containers contain at most 10 ml of the preparation, unless otherwise justified and authorised.

TESTS

Particle size. Unless otherwise justified and authorised, eye-drops in the form of a suspension comply with the following test: introduce a suitable quantity of the suspension into a counting cell or with a micropipette onto a slide, as appropriate, and scan under a microscope an area corresponding to 10 µg of the solid phase. For practical reasons, it is recommended that the whole sample is first scanned at low magnification (e.g. × 50) and particles greater than 25 µm are identified. These larger particles can then be measured at a larger magnification (e.g. × 200 to × 500). For each 10 µg of solid active substance, not more than 20 particles have a maximum dimension greater than 25 µm, and not more than 2 of these particles have a maximum dimension greater than 50 µm. None of the particles has a maximum dimension greater than 90 µm.

LABELLING

The label states for multidose containers, the period after opening the container after which the contents must not be used. This period does not exceed 4 weeks, unless otherwise justified and authorised.

Eye lotions

DEFINITION

Eye lotions are sterile aqueous solutions intended for use in washing or bathing the eye or for impregnating eye dressings.

Eye lotions may contain excipients, for example to adjust the tonicity or the viscosity of the preparation or to adjust or stabilise the pH. These substances do not adversely affect the intended action or, at the concentrations used, cause undue local irritation.

Eye lotions supplied in multidose containers contain a suitable antimicrobial preservative in appropriate concentration except when the preparation itself has adequate antimicrobial properties. The antimicrobial preservative chosen is compatible with the other ingredients of the preparation and remains effective throughout the period of time during which the eye lotions are in use.

If eye lotions are prescribed without an antimicrobial preservative, they are supplied in single-dose containers. Eye lotions intended for use in surgical procedures or in first-aid treatment do not contain an antimicrobial preservative and are supplied in single-dose containers.

Eye lotions examined under suitable conditions of visibility, are practically clear and practically free from particles.

The containers for multidose preparations do not contain more than 200 ml of eye lotion, unless otherwise justified and authorised.

LABELLING

The label states:

- where applicable, that the contents are to be used on one occasion only.
- for multidose preparations, the period after opening the container after which the contents must not be used. This period does not exceed 4 weeks, unless otherwise justified and authorised.

Powders for eye-drops and powders for eye lotions

DEFINITION

Powders for the preparation of eye-drops and eye lotions are supplied in a dry, sterile form to be dissolved or suspended in an appropriate liquid vehicle at the time of administration.
They may contain excipients to facilitate dissolution or dispersion, to prevent caking, to adjust the tonicity, to adjust or stabilise the pH or to stabilise the preparation.

After dissolution or suspension in the prescribed liquid, they comply with the requirements for eye-drops or eye lotions, as appropriate.

**TESTS**

**Uniformity of content** (2.9.6). Unless otherwise prescribed or justified and authorised, single-dose powders for eye-drops and eye lotions with a content of active substance less than 2 mg or less than 2 per cent of the total mass comply with test B for uniformity of content of single-dose preparations. If the preparation has more than one active substance, the requirement applies only to those substances which correspond to the above condition.

**Uniformity of mass** (2.9.5). Single-dose powders for eye-drops and eye lotions comply with the test for uniformity of mass of single-dose preparations. If the test for uniformity of content is prescribed for all the active substances, the test for uniformity of mass is not required.

**Semi-solid eye preparations**

**DEFINITION**

Semi-solid eye preparations are sterile ointments, creams or gels intended for application to the conjunctiva. They contain one or more active substances dissolved or dispersed in a suitable basis. They have a homogeneous appearance.

Semi-solid eye preparations comply with the requirements of the monograph on Semi-solid preparations for cutaneous application (0132). The basis is non-irritant to the conjunctiva.

Semi-solid eye preparations are packed in small, sterilised collapsible tubes fitted or provided with a cannula and having a content of not more than 5 g of the preparation. The tubes must be well-closed to prevent microbial contamination. Semi-solid eye preparations may also be packed in suitably designed single-dose containers. The containers, or the nozzles of tubes, are of such a shape as to facilitate administration without contamination. Tubes are tamper-proof.

**TESTS**

**Particle size.** Semi-solid eye preparations containing dispersed solid particles comply with the following test: spread gently a quantity of the preparation corresponding to at least 10 µg of solid active substance as a thin layer. Scan under a microscope the whole area of the sample. For practical reasons, it is recommended that the whole sample is first scanned at a small magnification (e.g. ×50) and particles greater than 25 µm are identified. These larger particles can then be measured at a larger magnification (e.g. ×200 to ×500). For each 10 µg of solid active substance, not more than 20 particles have a maximum dimension greater than 25 µm, and not more than 2 of these particles have a maximum dimension greater than 50 µm. None of the particles has a maximum dimension greater than 90 µm.

**Ophthalmic inserts**

**DEFINITION**

Ophthalmic inserts are sterile, solid or semi-solid preparations of suitable size and shape, designed to be inserted in the conjunctival sac, to produce an ocular effect. They generally consist of a reservoir of active substance embedded in a matrix or bounded by a rate-controlling membrane. The active substance, which is more or less soluble in physiological fluids, is released over a determined period of time.

Ophthalmic inserts are individually distributed into sterile containers.

**PRODUCTION**

In the manufacture of ophthalmic inserts, means must be taken to ensure a suitable dissolution behaviour.

**TESTS**

**Uniformity of content** (2.9.6). Ophthalmic inserts comply, where applicable, with test A for uniformity of content.

**LABELLING**

The label states:
- where applicable, the total quantity of active substance per insert,
- where applicable, the dose released per unit time.

01/2005:1105

**FOAMS, MEDICATED**

**Musci medicati**

Additional requirements for medicated foams may be found, where appropriate, in other general monographs, for example on Rectal preparations (1145), Vaginal preparations (1164) and Liquid preparations for cutaneous application (0927).

**DEFINITION**

Medicated foams are preparations consisting of large volumes of gas dispersed in a liquid generally containing one or more active substances, a surfactant ensuring their formation and various other excipients. Medicated foams are usually intended for application to the skin or mucous membranes.

Medicated foams are usually formed at the time of administration from a liquid preparation in a pressurised container. The container is equipped with a device consisting of a valve and a push button suitable for the delivery of the foam.

Medicated foams intended for use on severely injured skin and on large open wounds are sterile.

Medicated foams supplied in pressurised containers comply with the requirements of the monograph on Pressurised pharmaceutical preparations (0523).

**PRODUCTION**

Sterile medicated foams are prepared using materials and methods designed to ensure sterility and to avoid the introduction of contaminants and the growth of micro-organisms; recommendations on this aspect are provided in the text on Methods of preparation of sterile products (5.1.1).

**TESTS**

**Relative foam density.** Maintain the container at about 25 °C for at least 24 h. Taking care not to warm the container, fit a rigid tube 70 mm to 100 mm long and about 1 mm in internal diameter onto the push button. Shake the container to homogenise the liquid phase of the contents and dispense 5 ml to 10 ml of foam to waste. Tare a flat-bottomed dish with a volume of about 60 ml and about 35 mm high. Place the end of the rigid tube attached to the push button in the corner of the dish, press the push button and fill the dish uniformly, using a circular motion. After the foam has