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Ophthalmic optics — Contact lens care products — Guidelines for determination of shelf-life

Optique opthalmique — Produits d'entretien pour lentilles de contact — Lignes directrices pour la détermination de la durée de conservation

Reference number
ISO 13212:1999(E)

Foreword

ISO (the International Organization for Standardization) is a worldwide federation of national standards bodies (ISO member bodies). The work of preparing International Standards is normally carried out through ISO technical committees. Each member body interested in a subject for which a technical committee has been established has the right to be represented on that committee. International organizations, governmental and non-governmental, in liaison with ISO, also take part in the work. ISO collaborates closely with the International Electrotechnical Commission (IEC) on all matters of electrotechnical standardization.

International Standards are drafted in accordance with the rules given in the ISO/IEC Directives, Part 3.

Draft International Standards adopted by the technical committees are circulated to the member bodies for voting. Publication as an International Standard requires approval by at least 75 % of the member bodies casting a vote.

International Standard ISO 13212 was prepared by Technical Committee ISO/TC 172, *Optics and optical instruments*, Subcommittee SC 7, *Ophthalmic optics and instruments*.

Annex A of this International Standard is for information only.

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Introduction

The purpose of stability tests of contact lens care products is to obtain sufficient information to enable the manufacturer to establish an appropriate shelf-life and identify any unique storage conditions required to appear on the labelling for the product.

The quality of a contact lens care product is determined by its content of active ingredient(s), its purity and its physicochemical and microbiological properties. Due account should be taken of possible interaction of the container/closure with the contents.

The stability studies should ascertain how the quality of a product varies as a function of time and under the influence of a variety of environmental factors.

On the basis of the information thus obtained, storage conditions are recommended which will guarantee maintenance of the quality of the product, in relation to its safety, performance and acceptability, throughout the proposed shelf-life.

The design of the finished-product stability studies for a contact lens care product is based on knowledge obtained from studies on the active ingredient(s) and from the development studies.

Ophthalmic optics — Contact lens care products — Guidelines for determination of shelf-life

1 Scope

This International Standard provides guidance on the design of stability studies to use in gathering information to allow determination of shelf-life of contact lens care products.

This International Standard does not address studies designed to obtain information to establish the in-use stability (i.e. discard statement) of contact lens care products.

2 Normative references

The following normative documents contain provisions which, through reference in this text, constitute provisions of this International Standard. For dated references, subsequent amendments to, or revisions of, any of these publications do not apply. However, parties to agreements based on this International Standard are encouraged to investigate the possibility of applying the most recent editions of the normative documents indicated below. For undated references, the latest edition of the normative document referred to applies. Members of ISO and IEC maintain registers of currently valid International Standards.

ISO 8320-1, *Contact lenses and contact lens care products — Vocabulary — Part 1: Contact lenses.*

ISO 8320-2, *Contact lenses and contact lens care products — Vocabulary — Part 2: Contact lens care products.*

ISO 14534:1997, *Ophthalmic optics — Contact lenses and contact lens care products — Fundamental requirements.*

ISO14729[1)], *Ophthalmic optics — Contact lens care products — Microbiological requirements for products and regimens for hygienic management of contact lenses.*

ISO 14730[1)], *Ophthalmic optics — Contact lenses and contact lens care products — Antimicrobial preservative efficacy testing and discard dating of multi-dose preserved contact lens care products.*

3 Terms and definitions

For the purposes of this International Standard, the terms and definitions given in ISO 8320-1 and ISO 8320-2 apply.

1) To be published.

4 Requirements

4.1 The specified shelf-life of the contact lens care product shall be based on the evaluation of the results of stability studies.

4.2 Analytical methods that have been validated and are stability-indicating shall be used to assay for active ingredients. Validation includes, but is not limited to, being able to differentiate between the active ingredient and its degradation products. The test methods used shall be fully described.

5 Determination of finished product stability

5.1 Objective

The objective of stability testing on contact lens care products is to provide data for determining the time period during which the product performance characteristics are maintained and to define appropriate storage conditions.

The design of the stability tests is based on the known properties of the active ingredient(s), the properties of the chosen formulation and recommendation for use of the product.

The relevant assay methods shall be determined prior to the start of the stability testing.

The specifications proposed at the time of manufacture and valid to the end of the proposed shelf-life shall reflect, as far as possible, the results of the stability studies, particularly in relation to any parameters which could have a bearing on performance and safety and product acceptability.

5.2 Study methods

5.2.1 General

Before starting stability studies, a suitable testing plan should be set up, taking into consideration the properties of the active ingredient(s) as well as the proposed mode of action of the care product.

5.2.2 Real-time studies

These studies should be carried out under a range of controlled test conditions, when applicable, which will enable the shelf-life and the product container label/package insert storage requirements to be defined. This will normally include studies which should allow the properties of the product at temperatures between 20 °C and 30 °C to be evaluated. However, 25 °C $\pm$ 2 °C should be used as the mean kinetic testing temperature.

For each study, the mean temperature, the ranges of temperature and the mean humidity, if applicable, shall be stated in the stability report.

These studies are intended to support the initial shelf-life request and, for shelf-life extensions, any changes that could significantly impact the safety and performance of the product (e.g. certain changes in formulation, packaging materials or manufacturing methods).

NOTE Real-time studies should be performed in conjunction with accelerated ageing studies to establish an initial shelf-life.

5.2.3 Studies under varying storage conditions

These studies shall be carried out to provide important additional information. They can fulfil a number of objectives, such as:

— to support the initial shelf-life request by complementing the limited results of early real-time studies, as decomposition, if it is occurring, is likely to be accelerated;

— to produce useful data at an early stage of development, to demonstrate the effects of adverse storage in the packaging and product, and to enable storage conditions and suitable labelling to be provided;

— to support a request to extend the shelf-life.

The various test conditions should be stated. Depending on the nature and objectives of the stability study, the following may need to be considered:

a) various test temperatures: three or more, particularly if long-term real-time data are unavailable. The effect of low temperature may in addition need to be considered, such as below –15 °C (freezer), 2 °C to 8 °C (refrigerator) and freeze-thaw cycling;

b) high humidity: relative humidity > 75 %. Storage under high humidity conditions applies particularly to solid dosage forms. For products such as solutions, suspensions, etc. contained in packs designed to provide a permanent barrier to water loss, storage under high humidity is not necessary. However, low humidity can adversely affect products packaged in semipermeable containers;

c) elevated temperature and humidity in combination: e.g. temperature of 40 °C associated with a relative humidity of 75 %, possibly the effects of cycling between different temperatures and humidities;

d) since most contact lens care products are water-based, relative humidity less than 40 %, for example, 25 °C and 35 % relative humidity, should be considered;

e) light: either natural daylight or defined artificial illumination.

An example of a stability-testing plan for the finished product is shown in annex A.

5.3 Description of the product under study

5.3.1 Number and nature of the batches tested

The number of batches tested shall be stated with the batch number, details of the composition, date of manufacture, size of the batch, and the batch number and name of the manufacturer of the active ingredient(s) used.

Normally, three batches of the finished product are studied. If the number of batches tested is less than three, it shall be justified.

Satisfactory performance of the product in the smallest size container and having highest surface/volume ratio shall allow the extension of shelf-life to containers which are up to eight times larger in volume.

5.3.2 Primary container

The product batches shall be packed in primary containers proposed for marketing. The smallest primary container size should be tested. Satisfactory performance in the smallest size shall allow marketing of the product in containers with eight times the volume present in the smallest size.

Details of the packaging should be stated, including:

a) type(s) of container and closure, and nature of the constituent material(s);

b) nature of any desiccant used;

c) listing of the complete range of sizes of the product proposed for marketing.

5.4 Characteristics

5.4.1 General

The characteristics studied should be:

a) those in the finished product specification that are likely to be affected by storage, and

b) those not monitored routinely at the time of manufacture, but which may be indicative of the stability/instability of the particular product, e.g. dissolution of tablets.

5.4.2 Physical characteristics of the finished product

The following physical characteristics should be tested:

a) physical properties specific to the product, such as hardness and hygroscopicity for tablets, or pH, color, clarity and viscosity for solutions;

b) important quality parameters, such as *in vitro* dissolution, moisture content (e.g. in relation to any desiccant used in the packaging), particle size;

c) any other physical characteristics of the product that must be known in order to assess product stability.

5.4.3 Microbial characteristics

The following microbial characteristics shall be tested:

a) antimicrobial activity of finished products to be marketed for chemical disinfection of contact lenses shall be tested in accordance with ISO 14729, unless otherwise justified;

b) preservative efficacy of preserved products shall be tested at the end of shelf-life, in accordance with ISO 14730, unless otherwise justified;

c) sterility of sterile products; or provide valid data to demonstrate maintenance of package integrity;

d) microbial limits of nonsterile products shall be given.

5.4.4 Chemical characteristics of the finished product

The following chemical characteristics should be determined:

a) assay of the active ingredient(s), when possible;

b) consideration of other agents (such as antimicrobial preservatives and antioxidants);

c) any other chemical characteristics that must be known in order to assess the quality of the product.

5.4.5 Characteristics of primary-container interactions

If necessary, carry out a study of the container and closure interaction with the contents in any case where this is a risk.

5.4.6 Performance characteristics

If stability cannot be established by chemical methods, it should be followed by relevant performance characteristics. Performance tests should mimic as closely as possible the in-use condition, or the rationale for the design of test(s) should be described.

5.5 Evaluation methods

The test procedures applied to the stability tests on the finished product shall be fully described and validated.

5.6 Presentation of results

The results shall be summarized (e.g. as tables and graphs). For each product batch tested, the initial results (at the time of manufacture) and the results obtained during storage should be given. Results of real-time data should be recorded as they become available, up to the proposed shelf-life.

5.7 Discussion, interpretation and conclusions

The discussion and conclusion shall provide a critical evaluation of the suitability of the test methods used, the results obtained and the proposed shelf-life specification. This should take into account the safety and performance requirements of the product at the end of shelf-life.

If it was necessary to carry out any further studies due to significant changes in relevant properties, an explanation should be given, together with the results of these studies.

A minimum of three months' real-time data at 25 °C should be available, supported by data from accelerated stability studies. Such data would not normally be expected to be suitable for prediction of a shelf-life in excess of two years. Any extension of the shelf-life should be based on additional real-time study results.

Studies under accelerated test conditions will increase the decomposition and may permit some extrapolation of the room temperature shelf-life from that which would otherwise be acceptable. However, such studies would always need to be supplemented by long-term real-time studies, and normally at least three months' real-time data should be available.

If product batches in test demonstrate a decreasing stability profile, the shelf-life proposed and any overage should be based on the stability of the least stable test result, unless an explanation can be given.

The shelf-life (expiration date) shall be proposed on the primary package to be used for sale.

If there is evidence that batches of the stored product as packed for sale are stable at temperature up to 30 °C, the product need bear no special temperature storage instructions. However, if there is evidence that the product must be stored under defined conditions of storage, this shall be stated on the container label and the package insert (if included) and the outer carton. The maximum (or minimum) storage temperature should be stated in degrees Celsius (e.g. store below 25 °C; store in a refrigerator at 2 °C to 8 °C; do not refrigerate — store above 8 °C). These label/package insert storage recommendations shall reflect conditions found in the country(ies) in which the product is to be placed on the market.

NOTE 1 Temperatures acceptable for accelerated extrapolation of the expiration date should maintain the same mechanism of decomposition. Generally, temperatures at or below 45 °C should be acceptable.

NOTE 2 For every 10 °C increase in temperature, the rate of decomposition generally increases by a factor of two. Unless otherwise justified based on kinetic evidence, this acceleration factor should be used.

5.8 Ongoing stability

Where data on routine production batches are not provided, ongoing stability studies should be carried out on at least two of the first production batches and the results recorded.