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Ophthalmic optics — Contact lenses and contact lens care products — Guidelines for determination of preservative uptake and release

Optique ophtalmique — Lentilles de contact et produits d'entretien pour lentilles de contact — Lignes directrices pour la détermination de l'absorption/adsorption et le relargage des conservateurs

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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 11986 was prepared by Technical Committee ISO/TC 172, *Optics and optical instruments*, Subcommittee SC 7, *Ophthalmic optics and instruments*.

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Introduction

Contact lens care products are a complex mixture of organic and inorganic substances. For reasons of microbiological safety, contact lens disinfecting solutions, as well as care products in multi-use containers, contain substances with antimicrobial activity. From many years of experience in contact lens wear, it is known that irritation and sensitization problems sometimes occur due to these preservatives being absorbed and released by the matrix of the contact lens. For these reasons, it is necessary to be able to estimate the extent of preservative uptake and release by contact lenses.

The preservative uptake and release test provides general guidance on measuring the uptake of preservatives in solution by contact lenses and the release of preservatives from contact lenses in an aqueous medium. The analytical method to be used for quantification of specific preservatives is not indicated here. Chemical characteristics of the preservative as well as concentration in the contact lens care product and degree of uptake by the contact lens must be taken into consideration in selecting an appropriate analytical method. Contact lens uptake and release data may be useful in characterizing the potential for a new or modified contact lens material to produce a toxic or irritating reaction in the eye from the uptake and binding or release of preservatives from currently marketed contact lens care products.

Ophthalmic optics — Contact lenses and contact lens care products — Guidelines for determination of preservative uptake and release

1 Scope

This International Standard provides guidance for the selection of methods, preparation of samples, and conduct of testing for the uptake and release of preservatives from contact lenses.

NOTE Due to the manifest difficulties of reproducibly coating contact lenses with mineral and organic deposits, these methods are only applicable to new and unused contact lenses.

2 Normative reference

The following normative document contains 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 edition of the normative document 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 10344, *Optics and optical instruments — Contact lenses — Saline solution for contact lens testing.*

3 Principle

The contact lenses to be tested are immersed in the test product at (25 ± 2) °C and the preservative content analyzed at regular intervals of time until a steady-state condition has been achieved.

After reaching the steady-state condition, each contact lens is immersed in 1 ml of ISO Standard saline solution (see ISO 10344) at (37 ± 2) °C for 15 h. The solution is analyzed for the amount of preservative that has been extracted.

4 Procedure

4.1 General

The following information shall be obtained before commencing the estimation:

a) evidence, that the selected test method is suitable for the detection and estimation of the particular preservative;

NOTE Examples of methods suitable for analyzing thiomersal, chlorhexidine and benzalkonium chloride are presented in US FDA guidelines (see reference [2]).

b) evidence, that the test method has the required repeatability and reproducibility and that the detection limit is within the specified criterion;

c) the number of determinators required to satisfy b);

NOTE Multiple determinations may be necessary when the analysis result is close to the limit of detection and/or when the analysis method has a low precision.

d) the criteria needed to confirm that equilibrium has been achieved in the extraction process;

e) the number of each type of contact lens to be used (at least five contact lenses of each material type will need to be taken to ensure that the quantity of absorbed and released preservative is higher than the detection limit of the method of analysis).

4.2 Uptake of preservatives from test product

4.2.1 Select the appropriate contact lens care product and/or the appropriate contact lens material for testing.

4.2.1.1 To determine the preservative uptake of a new or modified contact lens material, select the appropriate contact lens care product based on the intended use of the contact lens care product (e.g. recommended for use with hydrogel contact lenses, or rigid gas permeable contact lenses).

4.2.1.2 To determine the uptake of a new or modified preservative in the contact lens care product by contact lenses, select the appropriate contact lens materials for testing from currently marketed contact lenses based on the intended use of the contact lens care product (e.g. recommended for use with hydrogel contact lenses, or rigid gas permeable contact lenses).

NOTE The selection of test lenses and lens care products should be adequately justified. For hydrogel lenses, representative lenses from low water and medium/high water ionic and nonionic lens groupings should be included. For rigid lenses, representative lenses from silicone, fluorine and silicon-fluorine lens groups should be included (see ISO 11539).

4.2.2 Determine the initial preservative level in the test solution.

4.2.3 Record the volume of soak solution and immerse the test lenses in the test solution in a suitable vial (see note 1) at (25 ± 2) °C, and shake occasionally (to ensure adequate mixing of the solution surrounding the contact lens during the study). Take aliquot portions of the test solution at different time intervals of not less than 24 h, and analyze each for its preservative content. Continue the procedure until the aliquot portions show that no more preservative has been absorbed.

NOTE 1 It is preferable to use containers that have been demonstrated to only absorb insignificant amounts of the preservative. However, if the container does absorb the preservative, this should be allowed for when carrying out the test procedure. In this case, for example, an appropriate control solution without a contact lens should also be monitored to determine the amount of preservative absorbed by the container.

NOTE 2 Alternatively, the amount of preservative taken up by the contact lens may be determined directly by methods that allow quantitative extraction from the contact lens using a suitable solvent and measuring the amount of preservative found in the extraction solvent.

NOTE 3 If the aliquot portions taken are large enough to significantly alter the ratio between volume of the test solution and the mass of the test lenses, use additional test lenses and containers for each sampling interval.

NOTE 4 If a high percentage of the preservative is absorbed by the test lenses, it may be necessary to repeat the test with an increased ratio of test solution volume to number/mass of test lenses.

4.3 Release of preservatives from test lenses

Remove the test lenses from the test solution and remove excess solution by gently touching each test lens with an absorbent tissue without using excessive force or contact time.

Immerse one test lens in 1 ml of ISO Standard saline solution (see ISO 10344). Leave the test lenses immersed at (37 ± 2) °C for 15 h and shake occasionally.

Take aliquot portions of the solvent at different times and analyze each for its preservative content. Continue the procedure until the aliquot portions show that no more preservative has been extracted.

NOTE If the aliquot portions taken are large enough to significantly alter the ratio between volume of the test solution and the mass of the test lenses, use additional test lenses and containers for each sampling interval.

5 Expression of results

The quantity of preservative absorbed by the contact lenses shall be calculated either

a) from the difference between the preservative content in the test solution before the contact lenses were immersed, and the concentration in the test solution after reaching the equilibrium of the preservative uptake; or

b) by a direct measurement method of the quantitative amount of preservative taken up by the contact lens.

If no preservative uptake is detected, the results shall be expressed as a preservative uptake that is less than the limit of detection of the test method.

Preservative release from the contact lenses shall be calculated from the concentration of the preservative found in the extracting solvent after reaching steady-state.

In the test report these values shall be expressed as either:

a) micrograms of preservative per milligram of dry lens mass (for hydrogel contact lenses); or

b) micrograms of preservative per square centimetre of lens surface of non-hydrogel contact lenses.

6 Test report

The test report shall include at least the following information:

a) a reference to this International Standard, i.e. ISO 11986;

b) the identity of the contact lens used, including the lot numbers and the types of contact lens material;

c) the identity of the preservative, the concentration of the preservative in the test solution and the volume used;

d) the identity of the selected solvent used for the extraction;

e) the duration of soak time, the detection limit and the calibration curve for the analytical method;

f) the date of the test;

g) the results of the test as specified in clause 5.

Bibliography

[1] ISO 11539:—[1)], *Ophthalmic optics — Contact lenses — Method for classifying contact lenses and contact lens materials*.

[2] The Guidance For Industry, Premarket Notification (510(k)) *Guidance Document for Contact Lens Care Products*, U.S. Department of Health and Human Service, Food and Drug Administration, Center for Devices and Radiological Health, Chem. — Appendix A. Preservative Uptake/Release Testing Procedures, May 1, 1997, pp. 82-85.

1) To be published.