INTERNATIONAL STANDARD

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Ophthalmic optics — Contact lenses and contact lens care products — Determination of preservative uptake and release

Optique ophtalmique — Lentilles de contact et produits d'entretien pour lentilles de contact — Détermination de l'absorption/adsorption et du relargage des conservateurs

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Foreword

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International Standards are drafted in accordance with the rules given in the ISO/IEC Directives, Part 2.

The main task of technical committees is to prepare International Standards. 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.

Attention is drawn to the possibility that some of the elements of this document may be the subject of patent rights. ISO shall not be held responsible for identifying any or all such patent rights.

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

This second edition cancels and replaces the first edition (ISO 11986:1999), which has been technically revised.

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 a general method for 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 — Determination of preservative uptake and release

1 Scope

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

NOTE 1 Due to the manifest difficulties of reproducibility when coating contact lenses with mineral and organic deposits encountered during lens wear, these methods are only applicable to new and unused contact lenses.

NOTE 2 Preservative depletion by a contact lens in the limited volume of a lens case could compromise disinfection performance. This International Standard does not measure disinfection performance.

2 Normative references

The following referenced documents are indispensable for the application of this document. For dated references, only the edition cited applies. For undated references, the latest edition of the referenced document (including any amendments) applies.

ISO 18369-3:2006, *Ophthalmic optics — Contact lenses — Part 3: Measurement methods*

3 Principle

The contact lenses to be tested are immersed in the test product at 25 °C ± 2 °C and the preservative content analysed 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 saline solution for contact lens testing, the saline solution prepared in accordance with ISO 18369-3:2006, 4.7, at 37 °C ± 2 °C. At discrete intervals up to and including 16 h, and at intervals until no additional release is observed, if required, the solution is analysed for the amount of preservative that has been extracted at each time point.

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 1 Examples of methods suitable for analysing some preservatives are presented in US FDA guidelines (see Reference [2]).

b) evidence that the test method has the required repeatability and reproducibility, and a detection limit suitable for the assay;

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

NOTE 2 Multiple determinations might 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 amount of test solution taken will need to ensure that the quantity of absorbed preservative does not reduce the concentration of the preservative in the test solution to less than 25 % of the initial preservative concentration in the test solution;

f) a sufficient number of contact lenses of each material type shall be used to ensure that the quantity of absorbed and released preservative is higher than the detection limit of the method of analysis, and also ensure that enough lenses are available for preservative release measurement at each time point.

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, 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).

The selection of test lenses and lens care products should be justified. For hydrogel lenses, representatives from low water and medium/high water ionic and non-ionic lens groups and from silicone hydrogel lenses should be included. For rigid lenses, representative lenses from silicone, fluorine and silicon-fluorine lens groups should be included (see ISO 18369-1).

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 closed container (see the following paragraph) at 25 °C ± 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 and analyse each for its preservative content. During day 1, take aliquot portions at the proposed regimen time, at 8 h and at 24 h. Continue the procedure at intervals of not less than 24 h until the aliquot portions show that no more preservative has been absorbed, or the maximum recommended storage time for the lenses in the contact lens care products has been reached. Additional time points during the first day may be included to determine the uptake profile.

It is preferable to use containers that have been demonstrated to 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 should also be monitored to determine the amount of preservative absorbed by the container.

NOTE 1 Alternatively, the amount of preservative taken up by the contact lens can be determined directly by methods that provide reproducible quantitative extraction from the contact lens, using a suitable solvent and measuring the amount of preservative found in the extraction solvent.

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

NOTE 2 If the percentage of the preservative absorbed by the test lenses exceeds 75 % of the available preservative, it might be necessary to repeat the test with an increased ratio of the test solution volume to number/mass of test lenses.

4.3 Release of preservatives from test lenses

After reaching a steady-state condition (see 4.2.3), remove the test lenses from the test solution and remove any excess solution by gently touching each test lens with an absorbent tissue without using excessive force or contact time.

Immerse the test lenses in saline solution, prepared in accordance with ISO 18369-3:2006, 4.7, at a ratio of one lens per millilitre of saline solution, in a closed container. Leave the test lenses immersed at 37 °C ± 2 °C and shake occasionally.

Take aliquot portions of the solvent at different times and analyse each for its preservative content. Measure aliquot portions of the solvent at 1 h, 2 h, 4 h and 16 h and until no additional release (steady state) is observed.

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

If 1 ml of saline solution (see ISO 18369-3:2006, 4.7) is not sufficient to immerse the test lens, then an additional minimal known quantity of saline solution may be added to ensure that the lens is fully immersed, and the volume is recorded. The total volume of saline solution must be used to calculate the concentration of preservative in the extracting saline solution.

5 Expression of results

5.1 The quantity of preservative absorbed by the contact lenses at each measured time point shall be determined by either

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

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

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

5.3 The preservative uptake is calculated using each measured time point and plotted as the uptake of preservative versus time.

5.4 The rate of preservative uptake, K_n, shall be expressed for each time point from the following equation:

$$K_n = \frac{U_n - U_{n-1}}{t_n - t_{n-1}}$$

where

U_n is the quantity of preservative taken up at a time point;

U_{n-1} is the quantity of preservative taken up at the previous time point;

t_n is the time the lens has been immersed in the solution for measurement n;

t_{n-1} is the time the lens had been immersed in the solution in the previous measurement $n-1$.

Preservative release from the contact lenses shall be calculated from the concentration of the preservative found in the extracting solvent at each measured point and after reaching a steady state.

5.5 The quantity of preservative released is calculated using each measured time point and plotted as the release of preservative versus time.

5.6 The rate of preservative released, K'_n, at each time point shall be calculated using the following equation:

$$K'_n = \frac{R_n - R_{n-1}}{t_n - t_{n-1}}$$

where

R_n is the quantity of preservative released at a time point;

R_{n-1} is the quantity of preservative released at the previous time point;

t_n is the time the lens has been immersed in the solution for measurement n;

t_{n-1} is the time the lens had been immersed in the solution in the previous measurement $n-1$.

5.7 In the test report, preservative 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 lens, where the lens is a −3,00 D lens with maximum supplied diameter for all lenses, or

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

5.8 The rates of uptake and release shall be expressed as either

a) micrograms of preservative per unit time per lens, where the lens is a −3,00 D lens with maximum supplied diameter, or

b) micrograms of preservative per milligram of lens dry weight per unit time.

6 Test report

The test report shall include at least the following information:

a) a reference to this International Standard, i.e. ISO 11986:2010;

b) the identity of the contact lens used, including the lot numbers and the types of contact lens material (e.g. hydrogel material group or identification of a silicone hydrogel manufacturer);

c) the identity of the preservative used, its concentration and the volume of test solution used per number of lenses in the lens care solution test;

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.