INTERNATIONAL STANDARD

**ISO 11980**

First edition
1997-12-15

# Ophthalmic optics — Contact lenses and contact lens care products — Guidance for clinical investigations

*Optique ophtalmique — Lentilles de contact et produits d'entretien pour lentilles de contact — Lignes directrices pour les investigations cliniques*

## 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.

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 11980 was prepared by Technical Committee ISO/TC 172, *Optics and optical instruments*, Subcommittee SC 7, *Ophthalmic optics and instruments*.



Annexes A to D of this International Standard are for information only.



International Organization for Standardization
Case postale 56 • CH-1211 Genève 20 • Switzerland
Internet central@iso.ch
X.400 c=ch; a=400net; p=iso; o=isocs; s=central

Printed in Switzerland

## Introduction

Currently contact lenses and contact lens care products are regulated in different ways in different countries. This International Standard has been developed to encourage a global harmonization. It is hoped that the adoption of this International Standard will be yet another step toward Mutual Recognition. This International Standard could also be used as a basis to fulfil design elements of ISO 9001.

# Ophthalmic optics — Contact lenses and contact lens care products — Guidance for clinical investigations

## 1 Scope

This International Standard provides guidance for the clinical investigation of the safety and performance of contact lenses and contact lens care products.

## 2 Normative references

The following standards contain provisions which, through reference in this text, constitute provisions of this International Standard. At the time of publication, the editions indicated were valid. All standards are subject to revision, and parties to agreements based on this International Standard, are encouraged to investigate the possibility of applying the most recent editions of the standards indicated below. Members of IEC and ISO maintain registers of currently valid International Standards.



ISO 14155:1996 *Clinical investigation of medical devices*



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

NOTE This International Standard attempts to harmonize the recognized regulatory requirements for the generation of clinical data to meet the marketing requirements for contact lenses and contact lens care products around the world. However, national requirements vary greatly. Wherever national practice or regulations dictate some legal requirement, this requirement takes precedence over this International Standard.

Some examples of additional requirements /guidance documents are found in annex D.

## 3 Definitions

For the purposes of this International Standard, the definitions given in ISO 14155 and ISO 14534 apply.

NOTE Additional definitions can be found in ISO 8320-1 and ISO 8320-2 (see annex D).

## 4 General clinical investigational requirements

General requirements and guidance for a clinical investigation are given in ISO 14155.

The clinical investigator shall inform the sponsor, the monitor and national regulatory authorities, if applicable, about any severe adverse event and about all adverse device effects in a timely manner (ISO 14155).

The presence of severe adverse events requiring an immediate report are those that are considered sight-threatening or that may cause permanent tissue damage. These may include, but are not limited to, the following:

— corneal ulceration;

— corneal or conjunctival infection;

— severe inflammation (conjunctivitis, iritis);

— corneal scarring;

— permanent loss of vision.

All recorded adverse device effects shall be included in the final report.

## 5 Clinical investigational methodology

**5.1** General requirements and guidance for documentation, access to information, additional health care and clinical investigation plan are given in ISO 14155.

**5.2** The study shall be designed in such a manner as to minimize bias. Contact lenses and contact lens care products evaluated shall be chosen to provide a scientifically valid assessment of safety and performance in a representative population of users.

NOTE 1 The objective may include the simultaneous assessment of new contact lenses and new contact lens care products. In this class of investigation, safety and performance should relate to the system as a whole and not to the individual components.

NOTE 2 Elements of the study design, such as the number of eyes, number of subjects and the duration of the study, should include biometric considerations as a basis for this determination. The biometric planning may use information from sources such as peer-reviewed scientific literature, historical data or a pilot study. (Annex D contains informative references for consideration in clinical studies designed for contact lenses and contact lens care products.)



**5.3** Steps for assessing the compliance of contact lens wearers with the requirements of the clinical investigation plan shall be included in the plan.

**5.4** The clinical assessment of safety and performance of a contact lens or contact lens care product shall be based on valid scientific evidence that may include objective measurements and observations, and subjective responses obtained from a clinical investigation of the device for its intended purpose.

NOTE Procedures for obtaining clinical data using objective measurements and observations, and subjective responses from subjects participating in a clinical investigation of a contact lens or contact lens care product are given in annexes A and B.

## 6 Presentation of results

A final report of the clinical investigation shall be recorded. The report shall include a copy of the clinical investigation plan, data collection, data analysis together with a critical assessment of risks signed by the sponsor, and appropriate statistical analysis. The assessment of risks and benefits for signs, symptoms, problems and complaints shall be judged against valid scientific evidence from a concurrent control or from historical data, including the scientific literature.

The final report shall include:

a) accountability for all data from each centre and for all enrolled subjects, including those that have completed, were discontinued or remain active in the study at the time of the report. No subject shall be identifiable, either from the final report or published results;

b) discontinued subjects and reasons for discontinuations, given in separate tables;

c) accountability and reasons for the number of unscheduled lens replacements;

d) a list of subjects by the most recent lens-wearing experience and demographics before their enrolment in the clinical investigation;

e) a list of the average lens wear time for all subjects in the study;

f) a critical evaluation of all the data collected during the clinical investigation.

NOTE For sample reporting tables for the final report, see annex C.

# Annex A
(informative)

# Procedures for the evaluation of safety, physiological performance and effect on ocular tissues

## A.1 General

The following classifications should be considered whenever the procedure is included in the clinical investigation plan.

## A.2 Corneal oedema

### A.2.1 General

Corneal oedema should be classified separately for the epithelium and for the stroma.

### A.2.2 Epithelial oedema

Epithelial oedema should be classified according to the number of microcysts observed.



| | |
|---|---|
| 0 = None | No microcysts |
| 1 = Trace | 1 to 20 microcysts |
| 2 = Mild | 21 to 50 microcysts |
| 3 = Moderate | 51 to 100 microcysts |
| 4 = Severe | > 100 microcysts or bullae |



The presence/absence of vacuoles or bullae should be documented, along with their numbers. The presence of bullae should be considered as reportable grade 4 severe epithelial oedema.

### A.2.3 Stromal oedema

Stromal oedema should be classified according to the following scale:

| | |
|---|---|
| 0 = None | No oedema |
| 1 = Trace | Just detectable corneal clouding |
| 2 = Mild | Light density central corneal clouding (CC); borders distinct but visible only against pupil |
| 3 = Moderate | Very distinct borders on CCC or corneal striae |
| 4 = Severe | Dense CCC with distinct borders with corneal striae |

## A.3 Corneal infiltrates

Corneal infiltrates should be classified according to the following scale:

| | |
|---|---|
| 0 = None | No infiltrates |
| 1 = Trace | 1 to 5 epithelial infiltrates |
| 2 = Mild | 6 to 8 epithelial infiltrates |
| 3 = Moderate | > 8 epithelial infiltrates |
| 4 = Severe | Presence of stromal infiltrates |

## A.4 Endothelial regularity

Endothelial regularity should be classified according to the following scale:

0 = Regular endothelial mosaic
1 = Isolated difference in cell size
2 = Just noticeable variation in cell size or bumpiness of cell layer
3 = Easily detected difference in cell size or bumpiness of cell layer
4 = Noticeable cell layer bumpiness and loss of definition of cell borders

## A.5 Corneal vascularization

Maximal corneal vascularization should be reported according to the following scale:

| | |
|---|---|
| 0 = None | No vessel penetration |
| 1 = Trace | < 1,00 mm vessel penetration |
| 2 = Mild | ≥1,00 mm to ≤ 1,5 mm vessel penetration |
| 3 = Moderate | >1,5 mm to ≤ 2,00 mm vessel penetration |
| 4 = Severe | Vessel penetration > 2,0 mm |

Optionally the depth and location of vessel penetration can also be reported as follows:

Depth: a) superficial
b) stromal

Location:

| | | | |
|---|---|---|---|
| N | Nasal | T | Temporal |
| I | Inferior | S | Superior |
| C | Circumferential | X | Other (describe) |



## A.6 Corneal staining with fluorescein

Corneal staining should be recorded according to the following scale (see notes 1 and 2 below):

0 = None — No staining

1 = Trace — Minimal superficial staining or stippling
a) Dimpling, discrete dot staining, or
b) Trace superficial lens insertion marks or foreign body tracks

2 = Mild — Regional or diffuse punctate staining
a) Central or generalized, or
b) Peripheral including 3 - 9 o'clock staining, or
c) Foreign body tracks

3 = Moderate — Dense coalescent staining up to 2 mm in diameter
a) Corneal abrasion
b) Foreign body tracks

4 = Severe — Dense coalescent staining greater than 2 mm in diameter

The location of the staining observed should be recorded in the following manner. The preferred method for recording the location is by numbers (see figure A.1).

NOTE 1 — All corneal staining observations should be carried out using a blue stimulation light in conjunction with a yellow barrier filter in the observation system.

NOTE 2 — Recurrent erosion and corneal ulceration should be recorded under a section "Other complications".

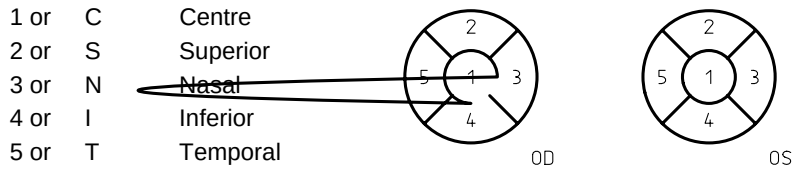


**Figure A.1 — Example of method for recording location of staining**

## A.7 Conjunctival observations

Limbal hyperaemia should be recorded on a 5-point scale as follows:

| | |
|---|---|
| 0 = None | No hyperaemia |
| 1 = Trace | Slight limbal (mild segmented) |
| 2 = Mild | Mild limbal (mild circumcorneal) |
| 3 = Moderate | Significant limbal (marked segmented) |
| 4 = Severe | Severe limbal (marked circumcorneal) |

Bulbar conjunctival hyperaemia should be recorded on a 5-point scale as follows:

| | |
|---|---|
| 0 = None | No hyperaemia |
| 1 = Trace | Slight regional hyperaemia |
| 2 = Mild | Diffuse hyperaemia |
| 3 = Moderate | Marked regional or diffuse hyperaemia |
| 4 = Severe | Diffuse episcleral or scleral hyperaemia |



Bulbar conjunctival compression/indentation (0 equals absence, 1 equals presence)



## A.8 Palpebral conjunctival observations

The location of maximal conjunctival response should be documented according to the following scale:

| | | |
|---|---|---|
| 0 = None | | Uniform satin appearance of the conjunctiva |
| 1 = Trace | | Slight conjunctival infection without texture |
| 2 = Mild | | Mild or scattered papillae/follicles less than 1 mm in diameter |
| 3 = Moderate | a) | Significant papillae/follicles less than 1 mm in diameter, and/or marked conjunctival infection |
| | b) | Staining of the top of one papilla |
| 4 = Severe | a) | Localized or generalized papillae/follicles 1 mm or more in diameter |
| | b) | Staining of the top of more than 1 papilla |

Optionally the conjunctival response can also be recorded for each of the four lid areas:

Upper lid
1 = Superior tarsal conjunctiva
2 = Middle tarsal conjunctiva
3 = Inferior (lid margin region) tarsal conjunctiva

Lower lid
4 = Palpebral conjunctiva of lower lid

# Annex B
(informative)

# Procedures for the evaluation of visual, refractive and lens performance and subject acceptance

## B.1 General

The following classifications should be considered whenever the procedure is included in the clinical investigation plan.

## B.2 Visual performance

To assess visual performance, visual acuity should be measured.

Optionally, low-contrast visual acuity, contrast sensitivity and visual performance measurement in the presence of a glare source may also be tested.

Traditionally, Snellen charts have been used to measure visual acuity, but they incorporate unequal steps between successive lines. The use of LogMAR progression visual acuity (VA) charts with equal steps between successive lines is recommended. Severe loss in visual performance should be a two-line or more loss on the LogMAR progression scale or its Snellen equivalent.



In those cases where a separate claim is made for a near-vision refractive effect, near-visual acuity using a reduced LogMAR or Snellen chart or reading a near chart should be recorded.



## B.3 Refractive performance

Refractive changes (absolute mean spherical and cylindrical values) from baseline to the final visit should be provided.

## B.4 Keratometric measurement

The keratometric findings should be reported as either the corneal radius and corneal astigmatism or the corneal radius in each principal meridian and the corneal astigmatism.

## B.5 Lens fitting characteristics

### B.5.1 General

The lens fitting characteristics should be assessed to evaluate the on-eye performance using the following classification:

### B.5.2 Lens centration

Lens centration for the eye in primary position (relaxed, looking straight ahead), should be recorded on a 3-point scale as follows:

0 = Optimal lens centration
1 = Acceptable decentration
2 = Unacceptable decentration