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Ophthalmic implants — Intraocular lenses —

Part 7: Clinical investigations

AMENDMENT 1

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AMENDEMENT 1

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Foreword

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Amendment 1 to ISO 11979-7:2006 was prepared by Technical Committee ISO/TC 172, *Optics and photonics*, Subcommittee SC 7, *Ophthalmic optics and instruments*.

Ophthalmic implants — Intraocular lenses —

Part 7:
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AMENDMENT 1

Page 13, Annex B

Replace the existing Annex B with the following:

ANNEX B
(informative)

Evaluation of post-operative adverse event and visual acuity rates

B.1 General

In order to allow for an uncontrolled study, rates of adverse events and visual acuity were taken from data in US studies to derive safety and performance endpoints (SPE).

B.2 Background

The data for the SPE rates were derived from weighted averages of the data from large clinical investigations of anterior and posterior chamber IOLs.

The data for posterior chamber IOLs were taken from eight clinical investigations of posterior chamber IOLs that were approved in the US (between December 1989 and December 1997). The pooled sample size for these clinical investigations was 4210 for adverse events and overall BCVA, and 3035 for best-case BCVA.

The data for anterior chamber IOLs were taken from five clinical investigations for anterior chamber IOLs that were approved in the US (between March 1988 and June 1991). The pooled sample size for these clinical investigations was 952 for adverse events and overall BCVA, and 635 for best-case BCVA.

B.3 Adverse event and visual acuity rates

The adverse event and visual acuity rates are provided in Tables B.1, B.2, B.3 and B.4. The terms used in the tables in this annex are defined as follows.

— SPE rate: safety and performance endpoint (rate derived from analysis of the data from clinical investigations of IOLs approved in the US).

— Maximum number of cases allowed before SPE rate exceeded: this is the maximum number of subjects with that adverse event that can occur in a clinical investigation before the rate in that investigation becomes statistically significantly greater than the SPE rate (see Tables B.1 and B.2).

— Minimum number of cases allowed before less than SPE rate: this is the minimum number of subjects with BCVA 0,3 logMAR or better that can occur in a clinical investigation before the rate in that investigation becomes statistically significantly less than the SPE rate (see Tables B.3 and B.4).

For adverse events not included in Annex B, comparison with published literature, previous clinical experience and the investigators' clinical judgement will determine acceptability.

Table B.1 — Anterior chamber IOL adverse event rates

Adverse event	SPE rate %	Number of subjects = 100 Max. number of cases allowed before SPE rate exceeded	Number of subjects = 300 Max. number of cases allowed before SPE rate exceeded
Cumulative:			
Cystoid macular oedema	10,0	15	39
Hypopyon	0,2	1	2
Endophthalmitis[a]	0,2	1	2
Lens dislocated from anterior chamber	1,1	3	6
Pupillary block	2,0	5	10
Retinal detachment	1,2	3	7
Secondary surgical intervention[b]	2,6	5	13
Persistent:			
Corneal stroma oedema	0,5	2	4
Cystoid macular oedema	3,8	7	17
Iritis	0,9	3	6
Raised IOP requiring treatment	2,1	5	11

[a] Endophthalmitis is defined as an inflammatory reaction (sterile or infectious) involving the vitreous body.

[b] Excludes posterior capsulotomies.

Table B.2 — Posterior chamber IOL adverse event rates

Adverse event	SPE rate %	Number of subjects = 100 Max. number of cases allowed before SPE rate exceeded	Number of subjects = 300 Max. number of cases allowed before SPE rate exceeded
Cumulative:			
Cystoid macular oedema	3,0	6	14
Hypopyon	0,3	1	3
Endophthalmitis[a]	0,1	1	1
Lens dislocated from posterior chamber	0,1	1	1
Pupillary block	0,1	1	1
Retinal detachment	0,3	1	3
Secondary surgical intervention[b]	0,8	2	5
Persistent:			
Corneal stroma oedema	0,3	1	3
Cystoid macular oedema	0,5	2	4
Iritis	0,3	1	3
Raised IOP requiring treatment	0,4	2	3

[a] Endophthalmitis is defined as an inflammatory reaction (sterile or infectious) involving the vitreous body.

[b] Excludes posterior capsulotomies.

Table B.3 — Overall post-operative BCVA 0,3 logMAR or better

Lens type	SPE rate %	Number of subjects = 100 Min. number of cases allowed before less than SPE rate	Number of subjects = 300 Min. number of cases allowed before less than SPE rate
Anterior chamber IOL	80,4	74	230
Posterior chamber IOL	92,5	88	270

Table B.4 — Best case post-operative BCVA 0,3 logMAR or better

Lens type	SPE rate %	Number of subjects = 100 Min. number of cases allowed before less than SPE rate	Number of subjects = 300 Min. number of cases allowed before less than SPE rate
Anterior chamber IOL	90,1	85	262
Posterior chamber IOL	96,7	94	285

EXAMPLE 1 In the case of “pupillary block” in Table B.1 for a 300-subject investigation, the SPE rate is 2,0 % and 10 is the maximum number of subjects allowed before the rate is significantly greater than the SPE rate (11 out of 300 is significantly greater than 2,0 %).

EXAMPLE 2 In the case of BCVA 0,3 logMAR or better in Table B.3 for a 300-subject investigation, the anterior chamber SPE rate is 80,4 % and 230 is the minimum number of cases allowed before the rate is statistically significantly less than the SPE rate (229 out of 300 is significantly less than 80,4 %).

B.4 Additional guidance

The following assumptions were used for Tables B.1 to B.4: Type I error = 0,05 with a one-sided alternative.

The calculated results for the adverse events (Tables B.1 and B.2) are based on using the binomial distribution, as mathematically described below, to test the null hypothesis that the true adverse event rate is less than or equal to the SPE rate. The alternative hypothesis would be that an adverse event rate is greater than the SPE rate. Similarly, for the best corrected visual acuity (Tables B.3 and B.4), the null hypothesis is that the true rate of cases with visual acuity 0,3 logMAR or better is greater than or equal to the SPE rate. The alternative hypothesis is that the “success” rate is less than the SPE rate.

For a given sample size, n, and SPE rate, p, the maximum number of adverse events allowed (before exceeding the SPE rate) can be obtained using the following equation.

$$\Pr\{X \geq x \mid n, p\} = 1 - \sum_{i=0}^{x-1} \binom{n}{i} p^i (1-p)^{n-i} \leq 0,05 \qquad \text{(B.1)}$$

where

p is the rate for the SPE;

n is the sample size;

x is the number of adverse events.

First, determine what is the minimum value of x for which Equation (B.1) is true (this is the smallest number of adverse events that will cause rejection of the null hypothesis). The maximum number of cases allowed (before significantly exceeding the SPE rate) is then $x - 1$.

The minimum number of allowable cases with BCVA 0,3 logMAR or better can be obtained using the following equation.

$$\Pr\{X \leq x \mid n, p\} = \sum_{i=0}^{x} \binom{n}{i} p^i (1-p)^{n-i} \leq 0,05 \qquad \text{(B.2)}$$

where

p is the rate for the SPE;

n is the sample size;

x is the number of cases with BCVA 0,3 logMAR or better.

First, determine what is the maximum value of x for which Equation (B.2) is true (this is the largest number of cases that will cause rejection of the null hypothesis). The minimum number of cases allowed (before being significantly less than the SPE rate) is then $x + 1$.