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Female condoms — Requirements and test methods

Préservatifs féminins — Exigences et méthodes d'essai

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Foreword

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The procedures used to develop this document and those intended for its further maintenance are described in the ISO/IEC Directives, Part 1. In particular the different approval criteria needed for the different types of ISO documents should be noted. This document was drafted in accordance with the editorial rules of the ISO/IEC Directives, Part 2 (see www.iso.org/directives).

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. Details of any patent rights identified during the development of the document will be in the Introduction and/or on the ISO list of patent declarations received (see www.iso.org/patents).

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For an explanation on the voluntary nature of standards, the meaning of ISO specific terms and expressions related to conformity assessment, as well as information about ISO's adherence to the World Trade Organization (WTO) principles in the Technical Barriers to Trade (TBT) see the following URL: www.iso.org/iso/foreword.html.

This document was prepared by Technical Committee ISO/TC 157, *Non-systemic contraceptives and STI barrier prophylactics*.

This third edition cancels and replaces the second edition (ISO 25841:2014) which has been technically revised.

The modifications are as follows:

— clinical failure mode definitions have been harmonized with ISO 29943-2;

— tolerances have been specified for the amount of lubricant applied to the female condom and the length, width and sheath thickness of the female condom. These tolerances are to be applied to the nominal values specified by the manufacturers for these design features;

— manufacturers are required to specify female condom width and thickness at three locations along the length of the female condom sheath;

— manufacturers are required to identify specifications and test methods as appropriate to verify the design and to ensure the quality and consistency of components and materials used for the retention features and any insertion feature used with the female condom;

— manufacturers are recommended to establish procedures for the periodic monitoring of microbial contamination (bioburden) as part of their quality management system including requirements for the absence of specific pathogens and limits for total viable counts on finished female condoms; methods of determining bioburden levels on female condoms are given in Annex I;

— detailed changes have been made to the test methods for determining freedom from holes and airburst properties to improve the reproducibility of female condom testing between laboratories and accommodate female condoms made from a wider range of sheath materials including sheaths made from natural rubber latex;

— a greater degree of harmonization with ISO 4074 has been achieved for common requirements and definitions;

— for female condoms with sheaths made from natural rubber latex, reference is included in the procedures for estimating provisional shelf lives from accelerated stability studies given in ISO 4074;

— the maximum lot size for female condoms has been limited to 500 000;

— labelling requirements have been revised and updated.

Introduction

A female condom is a sheath that completely lines the vaginal canal and is designed to be retained in the vagina during sexual intercourse and after withdrawal of the penis to prevent pregnancy and transmission of sexually transmitted infections (STIs).

A female condom is distinguished from a male condom in that it is retained in the vagina after withdrawal of the penis. The external component of the device can provide some coverage to the external female genitalia. Nonporous, intact, polymer films can be effective barriers to human immunodeficiency virus (HIV), other infectious agents responsible for the transmission of STIs and spermatozoa. Female condoms made from polymer films that are free from holes and defects, have adequate physical properties so as not to break during use, are correctly packaged to protect them during storage and are correctly labelled to facilitate their correct use, can be effective for contraceptive purposes and in the prevention of sexually transmitted infections (STIs).

To be safe, it is essential that the female condom and any lubricant, additive, dressing, individual packaging material or powder applied to it neither contain nor liberate substances in amounts that are toxic, sensitizing, locally irritating or otherwise harmful under normal conditions of storage or use.

Female condoms are non-sterile medical devices but manufacturers are advised to take appropriate precautions to minimize microbiological contamination of the product during manufacture and packaging. To ensure high quality products, it is essential that female condoms be designed and produced under a good quality management system. Reference can be made, for example, to ISO 9000, ISO 9004, ISO 9001, ISO 13485 and ISO 14971. To estimate the shelf life of any new or modified female condom, the manufacturer conducts stability tests before the product is placed on the market. This ensures that manufacturers have adequate data to support shelf-life claims and that these data are available for review by regulatory authorities, test laboratories and purchasers. They are also intended to limit the need for third parties to conduct long-term stability studies. Real-time shelf-life studies are also initiated, but not necessarily completed, prior to placing the product on the market.

Because female condoms are a relatively new class of device and designs of female condoms vary considerably, clinical investigations in humans are necessary to continue to build evidence of safety and efficacy. These investigations enable an assessment of the overall performance of internal and external retention features, failure modes, safety and effectiveness of female condoms. This document represents minimal requirements and test methods and acknowledges that new designs can require further due rigour of retention and other features as well as additional definition of specifications and test methods by the manufacturer.

All of these issues are addressed in this document.

Female condoms — Requirements and test methods

1 Scope

This document specifies the minimum requirements and test methods for female condoms that are supplied to consumers for contraceptive purposes and for assisting in the prevention of sexually transmitted infections (STIs).

2 Normative references

The following documents are referred to in the text in such a way that some or all of their content constitutes requirements 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 2859-1:1999, *Sampling procedures for inspection by attributes — Part 1: Sampling schemes indexed by acceptance quality limit (AQL) for lot-by-lot inspection*

ISO 4074, *Natural rubber latex male condoms — Requirements and test methods*

ISO 10993-1, *Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process*

ISO 10993-5, *Biological evaluation of medical devices — Part 5: Tests for in vitro cytotoxicity*

ISO 10993-10, *Biological evaluation of medical devices — Part 10: Tests for irritation and skin sensitization*

ISO 14155, *Clinical investigation of medical devices for human subjects — Good clinical practice*

ISO 14971, *Medical devices — Application of risk management to medical devices*

ISO 15223 (all parts), *Medical devices — Symbols to be used with medical device labels, labelling and information to be supplied*

ISO 29943-2, *Female condoms — Guidance on the design, execution, analysis and interpretation of clinical failure mode studies*

3 Terms and definitions

For the purposes of this document, the terms and definitions given in ISO 2859-1 and the following apply.

ISO and IEC maintain terminological databases for use in standardization at the following addresses:

— IEC Electropedia: available at http://www.electropedia.org/

— ISO Online browsing platform: available at http://www.iso.org/obp

3.1 General terms

3.1.1
acceptable quality limit
AQL
quality level that is the worst tolerable process average when a continuing series of *lots* (3.1.9) is submitted for acceptance sampling

[SOURCE: ISO 2859-1:1999, 3.1.26]

3.1.2
consumer package
package intended for distribution to a consumer, containing one or more *individual container(s)* (3.1.7) of *female condom* (3.1.5)

3.1.3
date of manufacture
date of formation of the *female condom* (3.1.5) sheath or the date the female condoms are packed in their *individual containers* (3.1.7) provided, in the latter case, a maximum period of bulk storage is specified and shelf-life studies have been conducted on female condoms that have been subjected to the maximum bulk storage period

3.1.4
expiry date
date after which the *female condom* (3.1.5) should not be used

3.1.5
female condom
sheath that completely lines the vaginal canal and is designed to be retained in the vagina during sexual intercourse and after withdrawal of the penis to prevent pregnancy and transmission of sexually transmitted infections

3.1.6
identification number
number, or combination of numbers, symbols or letters used by a manufacturer on *consumer packages* (3.1.2) to uniquely identify the *lot numbers* (3.1.10) of individual female condoms contained in that package and from which it is possible to trace those *lots* (3.1.9) through all stages of manufacturing, packaging and distribution

Note 1 to entry: When the consumer package contains only one kind of female condom, then the identification number can be the same as the lot number. However, if the consumer package contains several different types of female condoms, for instance, female condoms of different shapes or colours, then the identification number will be different from the lot number.

3.1.7
individual container
primary package containing a single *female condom* (3.1.5)

3.1.8
inspection level
index of the relative amount of inspection of an acceptance sampling scheme, chosen in advance and relating the sample size to the lot size

[SOURCE: ISO 3534-2:2006, 4.3.5]

3.1.9
lot
collection of *female condoms* (3.1.5) of the same design, colour, shape, size and formulation, manufactured at essentially the same time, using the same process, raw materials of the same specifications, common equipment and packed with the same lubricant and any other additive or dressing in the same type of *individual container* (3.1.7)

3.1.10
lot number
number or combination of numerals, symbols or letters used by the manufacturer to identify a *lot* (3.1.9) of individually packaged *female condoms* (3.1.5) and from which it is possible to trace that lot through all stages of manufacture up to packaging

3.1.11
non-visible hole
hole in a *female condom* (3.1.5) that is not visible under normal or corrected vision but is detected by a suitable water leakage test

Note 1 to entry: Leakage during testing can be detected, for instance, by rolling a female condom on absorbent paper.

Note 2 to entry: Suitable tests are specified in this document.

3.1.12
sampling plan
specific plan which indicates the number of units of product from each *lot* (3.1.9) that are to be inspected (sample size or series of sample sizes) and the associated criteria for determining the acceptability of the lot (acceptance and rejection numbers)

3.1.13
shelf life
period from *date of manufacture* (3.1.3) to the claimed *expiry date* (3.1.4) during which *female condoms* (3.1.5) are required to conform to the requirements for bursting pressure, bursting volume, freedom from holes and package integrity specified in this document

3.1.14
visible hole
hole or tear in the *female condom* (3.1.5) that is visible under normal or corrected vision before the condom is filled with water during the test for freedom from holes

3.1.15
visible defects
<condom, other than visible holes> broken, missing or severely distorted retention features, permanent crease with adhesion of the film or unintentional adhesion of the film to retention features including defect particles from *female condoms* (3.1.5) or other materials embedded in the female condom wall

3.1.16
visible defects
<individual containers> empty, leaking, damaged or dirty containers, illegible or missing information or absence of a notch or other device to facilitate opening the container without damaging the *female condom* (3.1.5) or rendering illegible any important information printed on the container

Note 1 to entry: Important information includes *lot number* (3.1.10), *expiry date* (3.1.4) and any instructions for use printed on the container.

3.2 Terms related to female condom failure modes

3.2.1
acute failure event
female condom (3.1.5) failure identified by the risk analysis conducted in accordance with ISO 14971

3.2.2
clinical breakage
female condom (3.1.5) breaks or tears during intercourse or withdrawal of the female condom from the vagina

Note 1 to entry: This might not be noticed until after inspection of the female condom following intercourse.

3.2.3
clinical breakage rate
number of *female condom* (3.1.5) broken or torn during sexual intercourse or withdrawal divided by the number of female condoms used during sexual intercourse

Note 1 to entry: Typically reported as a percentage.

3.2.4
non-clinical breakage
female condom (3.1.5) breakage that does not potentially expose the vagina to semen or other penile discharge

Note 1 to entry: An example of a non-clinical breakage is tearing a female condom while opening the package.

3.2.5
non-clinical breakage rate
number of *female condom* (3.1.5) broken that do not potentially expose the vagina to semen or other penile discharge divided by the number of female condom packages opened

Note 1 to entry: Typically reported as a percentage.

3.2.6
total breakage
sum of female condom *clinical* (3.2.2) and *non-clinical breakages* (3.2.4)

3.2.7
total breakage rate
number of *clinical* (3.2.2) and *non-clinical breakages* (3.2.4) divided by the number of female condom packages opened

Note 1 to entry: Typically reported as a percentage.

Note 2 to entry: The total breakage rate will not be the sum of the *clinical breakage rate* (3.2.3) and the *non-clinical breakage rate* (3.2.5). The clinical breakage rate has a different denominator than the other two rates.

3.2.8
clinical slippage
situation where the condom slips completely out of the vagina during sexual intercourse

3.2.9
clinical slippage rate
number of *female condoms* (3.1.5) that slipped divided by the number of female condoms used during sexual intercourse

Note 1 to entry: Typically reported as a percentage.

3.2.10
clinical misdirection
situation where the penis is inserted between the *female condom* (3.1.5) and the vaginal wall

3.2.11
clinical misdirection rate
number of *female condoms* (3.1.5) that misdirect divided by the number of female condoms used during sexual intercourse

Note 1 to entry: Typically reported as a percentage.

3.2.12
clinical invagination
external retention feature of the *female condom* (3.1.5) is partially or fully pushed into the vagina during sexual intercourse

3.2.13
clinical invagination rate
number of *female condoms* (3.1.5) that invaginate divided by the number of female condoms used during sexual intercourse

Note 1 to entry: Typically reported as a percentage.

3.2.14
total clinical failure
number of *female condoms* (3.1.5) with at least one *acute failure event* (3.2.1) that results in potential vaginal exposure to semen and other penile discharge

Note 1 to entry: Any female condom which experiences multiple clinical failure events only counts as a single clinical failure

Note 2 to entry: Includes female condoms with the following failures: *clinical breakage* (3.2.2), *slippage* (3.2.8), *misdirection* (3.2.10), *invagination* (3.2.12) or any failure event(s) in the risk assessment as described in 6.6.

3.2.15
total clinical failure rate
number of *female condoms* (3.1.5) with clinical failure divided by the number of female condoms used during sexual intercourse

Note 1 to entry: Typically reported as a percentage.

3.2.16
total female condom failure
female condom (3.1.5) with any type of clinical failure event or non-clinical failure event

3.2.17
total female condom failure rate
number of *female condoms* (3.1.5) with a clinical failure event or a non-clinical failure event divided by the number of female condom packages opened

Note 1 to entry: Typically reported as a percentage.

4 Quality verification

Female condoms are mass-produced articles manufactured in large quantities. Inevitably, there will be some variation between individual female condoms, and a small proportion of female condoms in each production run might not meet the requirements in this document. Further, the majority of the test methods described in this document are destructive. For these reasons, the only practicable method of assessing conformity with this document is by testing a representative sample from a lot or series of lots. Basic sampling plans are given in ISO 2859-1. Reference should be made to ISO/TR 8550-1 and ISO/TR 8550-2 for guidance on the use of acceptance sampling system, scheme or plan for the inspection of discrete items in lots. For testing purposes, sampling shall be conducted by lot number, not by identification number.

When ongoing verification is required of the quality of female condoms, it is suggested that, instead of concentrating solely on evaluation of the final product, attention is also directed at the manufacturer's quality system. In this connection, it should be noted that ISO 13485 covers the provision of an integrated quality system for the manufacture of medical devices.

Sampling plans shall be selected to provide an acceptable level of consumer protection. Suitable sampling plans are given in Annex A and Annex B.

— Annex A describes sampling plans based on ISO 2859-1 and is most applicable to manufacturers or purchasers assessing the conformity of a continuing series of lots. The full level of consumer protection available depends upon the switch to tightened inspection if deterioration in quality is detected. The switching rules, described in ISO 2859-1:1999, Clause 9, cannot offer their full protection for the first two lots tested but become progressively more effective as the number of lots in a series increases. The sampling plans in Annex A are recommended when five or more lots are being tested.

— Annex B describes sampling plans, based on ISO 2859-1, that are recommended for the assessment of isolated lots. The sampling plans in Annex B provide approximately the same level of consumer protection as those given in Annex A when used with the switching rules. It is recommended that

these sampling plans are used for the assessment of fewer than five lots, for example, in cases of dispute, for referee purposes, for type testing, for qualification purposes or for short runs of continuing lots.

It is necessary to know the lot size in order to derive from ISO 2859-1 the number of condoms to be tested. The lot size will vary between manufacturers and is regarded as part of the process and quality controls used by the manufacturer. If the lot size is not known or cannot be confirmed by the manufacturer, then a lot size of 500 000 condoms shall be assumed for determining the sample sizes for testing.

5 Lot size

The maximum individual lot size for production shall be 500 000 condoms.

This document does not specify the size of a lot, but it is possible for a purchaser to do so as part of the purchasing contract. Purchasers are encouraged to specify a lot size compatible with the manufacturer's quality management system.

6 Design

6.1 General

Female condoms shall be designed to prevent pregnancy and STIs during vaginal intercourse. A female condom is distinguished from a male condom in that it has an internal retention feature to prevent slippage and retain the female condom in the vagina after insertion and after withdrawal of the penis. A female condom also shall have an external retention feature to prevent invagination. A female condom may be made from natural rubber latex or synthetic materials.

The design of a female condom shall take into consideration the following:

a) product insertion into the vagina;

b) product retention and prevention of slippage during sexual intercourse or penile removal;

c) penile misdirection during sexual intercourse;

d) invagination of the female condom during sexual intercourse;

e) safe product removal after sexual intercourse;

f) the safety of all materials used in the construction of the female condom including the risk of any interaction between the materials;

g) the impermeability of the of the film to microorganisms;

h) the risk of breakage of the female condom during insertion, use and withdrawal.

6.2 Product insertion feature

Designs for female condoms shall include either a feature or tool to aid in the proper insertion and deployment of the female condom or methods for insertion of the female condom without such additional aids.

The insertion feature design, materials and/or method shall be evaluated for function as part of design validation and clinical evaluation of the finished female condom device described in Clause 9.

The insertion feature materials shall be evaluated for biocompatibility (irritation, sensitization, cytotoxicity and acute systemic toxicity) as an integrated feature of the finished female condom device in accordance with Clause 8.

Specifications and test methods as appropriate to verify the design and to ensure the quality and consistency of components and materials used for each insertion feature consistent with those used in the clinical trial described in Clause 9 shall be identified.

Examples of specifications the manufacturer should consider include critical dimensions, durometer (hardness), stiffness (modulus) and density.

6.3 Retention features

Designs for female condoms shall incorporate intra-vaginal retention features to retain the female condom within the vagina during sexual intercourse and permit safe withdrawal after use. Intra-vaginal retention features might be affixed on or placed within the sheath. Examples of intra-vaginal retention mechanisms include, but are not limited to, elastomeric rings and open or closed cell foam components.

Designs for female condoms shall incorporate external retention features to keep the open end of the female condom open during sexual intercourse, prevent misdirection of the penis and prevent female condom invagination. External retention features include but are not limited to annular, triangular or other-shaped components affixed to the open end of the female condom.

Retention feature designs, materials and/or methods shall be evaluated for function as part of design validation and clinical evaluation of the finished female condom device described in Clause 9 of this document. They shall also be evaluated in this manner to ensure the features stay affixed to the sheath or are retained within the sheath so that they remain intact during sexual intercourse and during product withdrawal, so that the features are completely removed from the vagina when the female condom is removed from the vagina.

Retention feature materials shall be evaluated for biocompatibility (irritation, sensitization, cytotoxicity and acute systemic toxicity) as an integrated feature of the finished female condom device in accordance with Clause 8.

The specifications and test methods required to verify the design and to ensure the quality and consistency of components and materials used for each retention feature shall be specified.

Examples of specifications that should be considered include critical dimensions, durometer (hardness), stiffness (modulus), bonding between the retention features and the sheath (if appropriate) and density.

Any of the critical requirements for the retention features that can change between lots shall be specified and appropriate test methods shall be described. The conformity level shall be an AQL of 2,5. The sampling plan shall be S-2.

6.4 Lubrication

The design of a female condom may include lubrication in any of the following manners:

a) lubricant pre-applied directly on the packaged female condom as supplied;

b) lubricant supplied in a separate container to be applied to the female condom by the user;

c) both pre-applied and as a separate container.

The type and amount of lubricant is unique to each female condom design. The nominal amount of lubricant consistent with amount of lubricant used in the clinical trial described in Clause 9 shall be specified. The specified amount of lubricant shall be based on the amount recovered using the test method specified in Annex C. This amount can differ significantly from the amount of lubricant added during manufacture, particularly if the internal retention feature is a sponge. The tolerance for the amount of lubricant shall be within ±15 % of the specified nominal amount.

When tested in accordance with the method given in Annex C, taking 13 female condoms from each lot, no female condom lubricant mass measurement shall be outside the specified range.

The specifications and test methods required to verify the design and to ensure the quality and consistency of the lubricant shall be specified. Examples of specifications the manufacturer should consider include viscosity.

Any lubricant supplied with or applied to the female condom in manufacture shall be compatible with the components used to manufacture the female condom. The compatibility of the female condom with representative examples of commonly used types of personal lubricants shall be evaluated and the product labelling or information provided with the female condom shall warn users of any common lubricant types that are not compatible with the female condom.

The lubricant shall be evaluated for biocompatibility (irritation, sensitization, cytotoxicity and acute systemic toxicity) as an integrated feature of the finished female condom device in accordance with Clause 8.

6.5 Dimensions

6.5.1 Length

The length of a female condom is unique to each design. The nominal length for the female condom, which shall be consistent with the length of the female condoms used in the clinical trial described in Clause 9, shall be specified. The maximum tolerance for length shall be ±5 mm if the nominal length is 150 mm or less, or ±10 mm if the nominal length is greater than 150 mm. When tested in accordance with the method given in Annex D, taking 13 female condoms from each lot, no female condom length measurement shall be outside the appropriate tolerance for the manufacturer's specified nominal length.

6.5.2 Width

The width of a female condom is unique to each design. The nominal width of the female condom, which shall be consistent with the width of the female condoms used in the clinical trial described in Clause 9, shall be specified. The nominal width shall be specified at positions 25 %, 50 % and 75 % along the length of the female condom from the closed end (based on the manufacturer's specified nominal length for the female condom). If because of the shape of the female condom it is not practical to determine the width at one or more of the specified positions, then the manufacturer may specify alternative positions that are as close as is practicably possible to these specified positions. The maximum tolerance for width requirements shall be ±2 mm. When tested in accordance with the method given in Annex E, taking 13 female condoms from each lot, no female condom width measurement shall be outside the manufacturer's tolerance for nominal width specified by the manufacture at each location.

6.5.3 Thickness

The thickness of a female condom is unique to each design. The nominal thickness of the female condom shall be specified. The nominal thickness shall be based upon the female condoms that were used in the clinical trial described in Clause 9. The nominal thickness shall be specified at positions 25 %, 50 % and 75 % along the length of the female condom from the closed end (based on the manufacturer's specified nominal length for the condom). If because of the shape of the female condom it is not practical to determine the thickness at one or more of the specified positions, then the manufacturer may specify alternative positions that are as close as is practicably possible to these specified positions. When tested by the method given in Annex F, taking 13 female condoms from each lot, the average thickness of each condom at each of the three locations along the length of the female condom shall be within ±15 % of the nominal thickness specified by the manufacturer for each of the three locations.

6.6 Risk assessment

A risk assessment for the product shall be conducted in accordance with ISO 14971. The assessment shall identify all potential failure modes for the device as well as any other safety and efficacy concerns. Failure modes identified in the risk analysis shall be compared to those listed in 3.2. In addition to these known failure modes, any new failure modes shall be assessed in the design and execution of any pre-clinical or clinical investigations of the female condom. The risk assessment shall include an

evaluation of compatibility of the female condom with representative types of commonly available personal lubricants.

7 Barrier properties

The barrier properties of the female condom shall be established by viral penetration studies using a suitable surrogate virus, for example, bacteriophage Phi-X174. When tested in accordance with the method given in Annex H, viral penetration properties shall be compared with those of a male latex condom that meets the requirements of ISO 4074 and exceeds 0,055 mm in thickness. Alternatively, a marketed female condom conforming to the requirements for 9.2 may be used as a comparator.

Studies conducted on male latex condoms having a minimum thickness of 0,055 mm that have been made by conventional dipping processes have confirmed that these products have effective barrier properties. Female condoms having a sheath made from natural rubber latex by conventional dipping processes with a thickness equal to or greater than 0,055 mm can be assumed to have acceptable viral barrier penetration resistance and are exempt from testing for conformity with this clause.

8 Biocompatibility

Biocompatibility for the finished product including any lubricant, additive, dressing material or powder applied to it shall be evaluated, as well as all retention or insertion devices whether affixed or removable. The individual components of the female condom may be assessed separately or the whole device may be assessed as a unit. If the individual components are assessed separately, then the final assessment of the finished female condom should be based on a weighted contribution to toxicity from each component.

Since the female condom is in repeat contact with surface mucosa and possibly compromised tissue surfaces, the testing shall be conducted to demonstrate that the materials are not cytotoxic nor cause sensitization or mucosal irritation in accordance with the relevant clauses of ISO 10993-1, ISO 10993-5 and ISO 10993-10. If there is a likelihood of systemic absorption of any components or residuals, further biocompatibility testing might be requested by regulatory authorities, such as acute systemic toxicity according to ISO 10993-11 and mutagenicity testing according to ISO 10993-3.

The laboratory used for any testing shall be accredited by a national accreditation body. The results shall be interpreted by a qualified toxicologist or any other appropriately qualified expert. The biological assessment report shall justify that the product is safe for its intended use.

Toxicity data on all additives and residual monomers, solvents and known impurities used in the manufacture of the female condom subject to this document shall be obtained. Suitable material safety data sheets shall be supplied on request for materials used in the manufacturer of products conforming to this document.

NOTE For female condoms made from natural rubber latex, many latex products that have been established as safe, including male condoms and medical gloves can exhibit a positive cytotoxic response when tested in accordance with ISO 10993-5. While any cytotoxic effect can be of concern, it is primarily an indication of potential for *in vivo* toxicity and a female condom cannot necessarily be determined to be unsuitable for use based solely on cytotoxicity data.

9 Clinical (human use) investigations

9.1 In order to assess the safety and effectiveness of a new female condom design, a contraceptive effectiveness study shall be conducted. The study design shall be adequate to allow the 6-month pregnancy rate to be computed using life table methods with at least 100 women years of data (e.g. 200 women completing six months). The 12-month pregnancy rate may be extrapolated from the 6-month data providing it is made clear that the value obtained is an estimate and the method of extrapolation is documented. The study should also measure all the rates of all failure modes identified in 3.2.

9.2 For new female condom designs that are sufficiently similar to a design that is already approved and marketed, the manufacturer may claim exemption from the requirement of 9.1. If a new female condom design and specifications are sufficiently similar to those of a marketed device and that marketed device has a known pregnancy rate established from a clinical effectiveness study, then the manufacturer may refer to the estimated pregnancy rate of the marketed device instead of conducting a contraceptive effectiveness study on the new device. If there is no suitable control female condom available in the market with an established pregnancy rate, then the manufacturer may use an alternative female condom that has been evaluated directly against a device with an established pregnancy rate as the control. To claim exemption from the requirements of 9.2, the following requirements shall be met.

a) A risk analysis according to 6.6 shall be conducted.

b) The design of a new female condom design and specifications shall be shown to be sufficiently similar to those of a marketed female condom, after assessing the impact of each difference in dimension, material, insertion and retention feature or method, on the incidence of each failure mode described in 3.2 on the incidence of new failure modes and on the efficacy of the female condom in preventing pregnancy and STI transmission. To be considered sufficiently similar to a marketed device, the risk analysis shall demonstrate that the new female condom can be expected to have the same failure modes as the marketed device and no new failure modes or other risk factors. The results of this assessment shall be made available to regulatory authorities.

   A randomized controlled clinical investigation comparing the new female condom to a control female condom shall be conducted in accordance with ISO 14155 and ISO 29943-2.

   NOTE Clinical investigations can also be subject to local regulatory requirements.

The following requirements shall apply to the clinical investigation.

— The control female condom shall meet the bursting volume and pressure, freedom from holes and visible defects and individual container integrity requirements of Clauses 11, 13, 14 and 15.1 and shall have a known pregnancy rate established from a clinical effectiveness study. If there is no suitable control female condom available in the market with an established pregnancy rate, then the manufacturer may use an alternative female condom that has been evaluated directly against a device with an established pregnancy rate as the control.

— The total clinical failure rate of the new female condom shall be shown to be non-inferior to the total clinical failure rate of the control female condom. The upper bound of the 95 % one-sided confidence interval for the new female condom total clinical failure rate minus the control female condom total clinical failure rate shall be less than or equal to 3 %.

— The upper bound shall be calculated using a method that accounts for the unique characteristics of data such as:

  — each study participant may contribute data from more than one female condom use, and

  — possibly low event rates.

  NOTE See Reference [35] for more information.

— The control female condom total clinical failure rates shall not be lower than 1 %. Rates lower than this would suggest that the study population is not typical of normal female condom users or there have been problems in identifying and/or reporting failures that occurred during the study.

10 Microbial contamination

The manufacturer is recommended to establish procedures for the control and periodic monitoring of microbial contamination (bioburden) as part of their quality management system. *Staphylococcus aureus, Pseudomonas aeruginosa* and *Enterobacteriaceae,* including *Escherichia coli*, are pathogenic organisms that can potentially be found on female condoms and can cause urinary tract or other infections. It is recommended that these organisms are absent from female condoms. The procedures

should include requirements for absence of specific pathogens and limits for total viable counts on finished female condoms. Methods of determining bioburden levels on female condoms are given in Annex I.

NOTE 1 General methods for determining microbial contamination on sterile medical devices are given in ISO 11737-1. The document includes methods for validating testing (ISO 11737-1:2006, Annex C). The methods described in Annex I have been found to be suitable for use with male and female condoms taking into account specific issues associated with testing these products. These issues include the residual antimicrobial activity of some compounds used in latex formulations that can interfere with the assays.

NOTE 2 To control microbial contamination on the finished product manufacturers need to control the manufacturing environment to reduce the risk of contaminating the product, establish general cleaning and sanitizing procedures throughout the operation and monitor bioburden levels on raw materials and equipment.

11 Bursting volume and pressure

11.1 Minimum values

The appropriate minimum pressure and volume limits for the specific female condom shall be specified based on the airburst properties of the lot or lots used for the clinical trial.

Products in the market prior to 15 July 2011, shall conform to the procedure in this subclause or may use existing specifications as established by their regulatory bodies for bursting properties. If the minimum pressure and volume limits have been set using an inflation rate different from that specified in Annex J, then the values shall be revalidated using the rate specified in Annex J.

The specifications shall be consistent with the requirements of this subclause based on a representative sample of the product tested at the time of the clinical trial. Information regarding the establishment of these values shall be made available to regulatory and governmental authorities upon request.

The following procedure shall be used.

a) Determine the airburst properties of the lot or lots used in the clinical study according to Annex J using a sample size of at least 2 000 female condoms. If more than one lot was used in the clinical study, then the sample shall be drawn across all the lots, each individual lot being sampled proportionally to its size.

b) Set the minimum airburst limits at 80 % of the 1,5 percentile values of the airburst volumes and pressures determined above (in this subclause). Round the bursting volume limit to the nearest 0,1 dm^3 if the value is 14,9 dm^3 or below and to the nearest 0,5 dm^3 if the value is greater than 14,9 dm^3. Round the bursting pressure to the nearest 0,05 kPa. After a period of production of at least 30 full scale manufacturing lots, the limits should be re-evaluated to confirm that they are still applicable.

NOTE Based on data supplied by manufacturers for both synthetic and natural rubber male latex condoms, taking 80 % of the 1,5 percentile values provides an adequate tolerance for the long-term lot-to-lot variability seen in normal manufacture.

For the purposes of this document, the relevant percentile, x, should be determined by ranking the N data values and taking the value of the n-th rank where $n = Nx/100 + 1/2$ rounded to the nearest integer (e.g. for N = 2 000, the lower 1,5 percentile is the 31st lowest value).

11.2 Sampling and requirements

Whenever tested by the methods given in Annex J, the bursting volumes and bursting pressures shall not be less than the minimum values established by the procedures described in 11.1. The conformity level shall be an AQL of 1,5 for non-conforming female condoms. A non-conforming female condom is defined as a female condom that fails the requirements for volume, pressure or both. Any female condom that exhibits any leakage during air-burst testing shall be replaced and testing continued.

Female condoms exhibiting leakage during air-burst testing shall not be counted as non-conforming, nor count towards the total number of female condoms tested.

12 Tests for stability and shelf life

12.1 General

The female condom shall conform to the airburst, freedom from holes, visible defects and individual container integrity requirements of Clauses 11, 13, 14 and 15.1 until the end of the labelled shelf life. Shelf-life claims shall not exceed five years from the date of manufacture.

NOTE A practical limit of five years has been set for the shelf life because manufacturers have no control over storage conditions once female condoms have been distributed.

The date of manufacture can be the date of sheath manufacture or the date of assembly and packaging of the female condom in individual sealed containers, depending upon the procedures specified by the manufacturer. The date of manufacture shall not exceed two years from the date of sheath manufacture. Unprocessed sheaths and/or unpackaged female condoms shall be stored under controlled conditions as specified by the manufacturer between sheath manufacture and packaging. Manufacturers shall have documented procedures for validating the storage conditions and maximum storage period. The stored sheaths and/or female condoms shall be protected from exposure to excessive temperatures, light, ozone and any other factor that could affect the shelf life of the packaged female condoms.

Data supporting the shelf-life claims shall be made available to the appropriate regulatory authorities and direct purchasers upon request.

Before a new or modified female condom design is placed on the market, the following requirements shall be met.

a) A real-time stability study as described in 12.2 to determine shelf life shall have commenced.

b) Pending completion of the real-time stability study, shelf life shall be estimated as described in 12.3.

For existing designs on the market prior to 15 July 2011, real-time data in a form consistent with Annex L, at a temperature of (30^{+5}_{-2}) °C shall be acceptable, to verify the shelf-life claims.

12.2 Procedure for determining shelf life by real-time stability studies

After testing in accordance with Annex L, the female condoms shall meet the requirements in Clauses 11, 13, 14 and 15.1

If the real-time data indicate a shorter shelf life than that claimed on the basis of accelerated ageing (see 12.3), the relevant regulatory authorities and direct purchasers shall be notified. The shelf life claim for the product shall be changed to one based on the real-time stability study. In no case shall shelf-life claim exceed five years. For female condoms placed on the market, real-time stability studies shall be completed for the full period of the shelf-life claim.

12.3 Procedure for estimating shelf life based upon accelerated stability studies

Pending the completion of real-time stability studies, accelerated stability studies shall be used to estimate the shelf life. Shelf life estimates shall be based on a mean kinetic temperature of (30^{+5}_{-2}) °C and relative humidity of (70 ± 5) % for all climatic conditions and may be carried out on female condoms from the same production lots as used for real-time determination of shelf life. For female condoms made from moisture resistant materials or packaged in moisture impermeable individual containers, such as aluminium foil laminate pouches, humidity control is not necessary.

Several approaches to the analysis of accelerated-ageing data have been explored. However, at the date of publication, no single method of analysis was sufficiently validated or widely used to justify

its designation as a standard method. The manufacturer may refer to ISO 11346 (Arrhenius testing) or use other validated methods to conduct its accelerated shelf-life studies. It is anticipated that as manufacturers and regulatory agencies accumulate real-time data, a consensus method for the next revision of this document will be developed. Meanwhile, the results of accelerated-ageing data may be analysed by a number of methods or as stipulated by the manufacturer's regulatory authority.

NOTE Arrhenius testing might not be applicable for some types of materials used for the manufacture of female condoms. The procedures for estimating shelf lives for male latex condoms by accelerated stability studies given in ISO 4074 might also be applicable to female condoms made from natural rubber latex. Subject to suitable validation procedures, the manufacturer could use similar procedures.

Guidance on the conduct and analysis of accelerated ageing studies is provided in Annex M. Data generated from such studies shall support the claim that the female condoms fulfil the requirements in Clauses 11, 13, 14 and 15.1 for the duration of the labelled shelf life and at a mean kinetic temperature of (30^{+5}_{-2}) °C.

13 Freedom from holes

When female condoms are tested for freedom from holes in accordance with the method described in Annex K, the conformity level shall be an AQL of 0,25 and the inspection level established in Annex A shall apply. Female condoms with non-visible holes in any position greater than 25 mm from the open end and visible holes in any position along the whole length of the sheath are considered non-conforming.

14 Visible defects

When female condoms are tested for visible defects as described in Annex K, the conformity level shall be an AQL of 0,4 and the inspection level established in Annex A shall apply.

15 Packaging and labelling

15.1 Individual container integrity

When female condom individual container integrity is tested in accordance with Annex G, the conformity level shall be an AQL of 2,5 and inspection level established in Annex A shall apply.

15.2 Packaging

Each female condom shall be packed in an individual, sealed container. One or more individual containers may be packed in other packaging such as a consumer package. The individual container, or consumer package or both, shall be opaque to light unless the female condom is manufactured from a material that is not affected by light. The packaging shall protect the female condom from light even if only the individual container is provided to the consumer. If female condoms are intended to be supplied only in individual containers, the individual containers shall be opaque unless the female condom is manufactured from a material that is not affected by light.

If a marking medium, such as ink, is used on a female condom or on any part of an individual container directly in contact with a female condom, it shall not have any deleterious effect on the female condom or be harmful to the user.

Individual containers and any other packaging shall protect the female condom from damage or loss of lubricant during normal transportation and storage.

Individual containers and any other packaging shall be designed in such a way that the package can be opened without damaging the female condom. The design of the individual container should facilitate easy opening.

15.3 Labelling

15.3.1 Symbols

If symbols are used on packaging, information and marketing materials, the symbols shall meet the requirements in ISO 15223. If symbols are used on the outside of the consumer packaging, their meaning should be explained in the additional information on the inside of the consumer package or a leaflet contained within the consumer package.

15.3.2 Individual containers

Each individual container shall be indelibly marked with the following information:

a) the identity of the manufacturer or distributor or, if permitted by local regulations, the registered brand or trademark;

b) the manufacturer's identifying reference for traceability (e.g. the lot number);

c) the expiry date (year and month). The format of the year shall be in four digits; the format of the month shall be in letters or two digits;

d) any additional marking required by local regulations.

NOTE For female condoms intended for distribution within the European Union, additional marking includes the CE Mark. Refer to EN 1041 for additional requirements for female condoms intended for distribution within the European Union.

15.3.3 Consumer packages

The outside of the consumer package shall bear at least the following information in at least one of the official language(s) of the country of destination or as stipulated differently by that country.

a) A statement of identity and intended use, for example, "A female condom is designed to be retained in the vagina during sexual intercourse to prevent pregnancy and transmission of sexually transmitted infections".

b) A statement of optimal use that provides specific instructions and/or diagrams on correct use, including how to insert and remove the female condom.

c) A statement of limitations, "No barrier methods, including male condoms or female condoms, provide 100 % protection against pregnancy and STIs".

d) A full description of the female condom. If the female condom is coloured or natural, textured or plain, has a flavour or fragrance and is lubricated or not, this shall be stated. A diagram may be used to convey some of this information.

e) The number of female condoms contained.

f) Size designation, if the manufacturer makes more than one size.

g) The name or trade name and full postal address of the manufacturer and/or distributor and/or manufacturer's authorized representative, depending on national and regional requirements. A PO box number is not an acceptable address.

NOTE For female condoms intended for distribution within the European Union, the name or trade name and address of the manufacturer is required. Where the manufacturer does not have a registered place of business in the European Union, the name and address of the European Authorized Representative is also required.

h) The expiry date (year and month). The format of the year shall be in four digits and the format of the month shall be in letters or two digits. If a consumer package includes female condoms from different lots, the earliest expiry date shall apply to all female condoms.

i) A statement of appropriate storage conditions for the female condom. Accepted symbols may be used as an alternative.

j) If the individual containers are not opaque to light and the product can be affected by light, a statement that individual containers shall not be stored outside the opaque consumer package.

k) Whether the female condom is lubricated or dry. Whenever a medicinal ingredient is added, it shall be identified and its purpose indicated (e.g. spermicidal). If the female condom or lubricant is fragranced or flavoured, this shall be stated.

l) The manufacturer's identifying reference for traceability (e.g. the identification number/lot number). If different types of female condoms, e.g. different colours, are packaged together in the same consumer package, the identification number on the consumer package shall allow the manufacturer to identify uniquely the lot numbers of the individual female condoms contained in that package, so that it is possible to trace lots through all stages of manufacture up to packaging.

m) If the female condom is made of natural rubber latex, a statement that the female condom is made of natural rubber latex, which might cause allergic reactions including anaphylactic shock if the user is allergic to latex. An accepted symbol for natural rubber latex may be used as an alternative. If a symbol is used, the additional information on the inside of the consumer package or a leaflet contained within the consumer packaging shall include a statement warning about the risk of allergic reactions including anaphylactic shock.

n) For female condoms intended for distribution within the European Union, the CE Mark.

o) A statement that the female condom is for single use only. An accepted symbol may be used as an alternative.

p) A statement to read the instructions for use. An accepted symbol may be used as an alternative.

15.3.4 Additional information for the consumer

The outside or the inside of the consumer package or a leaflet contained within the consumer package shall bear at least the following information expressed in simple terms and in at least one of the official language(s) of the country of destination. If possible, this should also be supplemented by pictorial representations of the major steps involved or as stipulated differently by that country.

a) Instructions for use of the female condom, including:

   1) the need to handle the female condom carefully, including removal from the individual container so as to avoid damage to the female condom by fingernails, jewellery, etc.;

   2) how and when to insert the female condom; mention shall be made that the female condom should be inserted into the vagina before any contact occurs between the vagina and the partner's body to assist in the prevention of STIs and pregnancy;

   3) if an additional lubricant is desired, a statement instructing the user to use only the correct type of lubricant which is recommended for use with the female condom;

   4) if the female condom is made with natural rubber latex, a statement instructing the user to avoid use of oil-based lubricants such as petroleum jelly, baby oil, body lotions, massage oils, butter, margarine, etc. as these are deleterious to the integrity of the female condom. For female condoms made from other materials, a statement warning of any incompatible lubricants that should not be used with the female condom;

   5) a statement instructing the user to consult a doctor or pharmacist about the compatibility of topical medicines that might come in contact with the female condom;

   6) advice to seek medical assistance as soon as possible, at least within 72 h should a female condom break, slip or leak during use;

7) advice that if the individual container is obviously damaged to discard that female condom and use a new one from an undamaged individual container;

8) instructions for withdrawal.

b) Instructions on how to dispose of the used female condom.

c) A statement that the female condom is for single use only and that cleaning and reuse can compromise the integrity of the device.

d) An explanation of any symbol used on the packaging.

e) If a symbol for latex is used on the packaging [as an alternative to the statement specified in 15.3.3 m)], a statement that the female condom is made of natural rubber latex, which might cause allergic reactions including anaphylactic shock if the user is allergic to latex.

f) The date of issue or the date of latest revision of the instructions for use.

g) If the product is manufactured to conform to all requirements of this document, the number of this document, i.e. ISO 25841.

h) For female condoms intended for distribution within the European Union, the CE Mark.

15.3.5 Female condoms not distributed in consumer packages

For female condoms that are distributed without a consumer package (e.g. in single packages), it is the responsibility of the organization distributing the female condoms to ensure that the information specified in 15.3.3 and 15.3.4 is supplied to the user in accordance with local regulations.

NOTE 1 In the European Union, the labelling of medical devices is subject to specific regulations.

NOTE 2 In countries outside of Europe, information could be in the form of leaflets, training sessions, posters or additional packing added in the distribution chain, subject to local regulations.

15.4 Inspection

When inspected, 13 consumer packages and 13 individual containers shall be selected from each lot and examined for conformity to 15.1, 15.2 and 15.3. All inspected containers shall conform to these requirements.

Under certain conditions, the manufacturer/distributor may correct faults associated with packaging and labelling requirements and resubmit the lot for further conformity testing. Examples include insertion of missing instruction leaflets or re-packaging of individual containers into new complete consumer packages before placing on the market.

If female condoms from the same lot are packed into different consumer packages, then at least one consumer package of each variant should be inspected. The number of packages inspected should not exceed 13 unless the number of variants exceeds 13.

16 Data sheets

A data sheet for each product variant that contains at least the following information shall be made available to all interested parties:

a) specifications for length, width and thickness;

b) the results of clinical trial lot air-burst testing. This includes the mean bursting volume, the mean bursting pressure and lower limits for bursting pressure and bursting volume as calculated in accordance with 11.1;

c) specifications for amount and type of lubricant or powder;

d) list of materials used in the product construction;

e) technical drawing(s) showing female condom geometry and correct locations of fixed retention features;

f) test methods and results for retention features;

g) details of any deviations from the test procedures and/or requirements specified in this document. Any such deviations shall be justified in the data sheet.

Annex A
(normative)

Sampling plans intended for assessing conformity of a continuing series of lots of sufficient number to allow the switching rules to be applied

A.1 Quality verification

When ongoing verification is required of the quality of female condoms, it is suggested that, instead of concentrating solely on evaluation of the final product, the party concerned also directs attention to the manufacturer's quality system. In this connection, it should be noted that ISO 9000- series and, in particular, ISO 13485 covers the provision of an integrated quality system.

A.2 Sampling plans and conformity levels

If a party wishes to establish, by inspection and testing of samples of the final product, whether a continuing series of lots are in conformity with the requirements of this document, the sampling plans and acceptance criteria given in Table A.1 shall be applied.

Manufacturers may use the schemes in Table A.1 or may devise and implement validated alternative quality control methods that result in at least equivalent consumer protection.

When tests are being conducted on fewer than five lots of female condoms, the additional protection of the switching rules in ISO 2859-1 is not available and it is recommended that the sampling plans given in Annex B are used to maintain the level of consumer protection.

Table A.1 — Sampling plans and acceptance criteria for a continuing series of lots

Attribute	Inspection level[a]	Acceptance criteria
Dimensions (including retention feature dimensions)	13 female condoms	All samples shall fall within the manufacturer's specified limits.
Bursting volume and pressure	General inspection level I	AQL of 1,5
Individual container integrity	Special inspection level S-3	AQL of 2,5
Freedom from holes	General inspection level I but at least code letter M	AQL of 0,25
Visible defects	General inspection level I but at least code letter M	AQL of 0,4
Packaging and labelling	13 consumer packages and 13 individual containers	All shall conform.
Quantity of lubricant	13 female condoms	All shall conform.
Retention feature properties	Special inspection level S-2	AQL of 2,5

[a] See ISO 2859-1 where relevant.

Applications for these sampling plans include the following:

a) ongoing production testing and quality control by a manufacturer;

b) ongoing testing by a purchaser for contractual purposes;

c) ongoing inspection by a national authority.

Annex B
(informative)

Sampling plans intended for assessing conformity of isolated lots

Use of the sampling plans given in Annex A for small numbers of lots, i.e. fewer than five, will result in a higher level of consumer risk because the switching rules are not available. In such circumstances, the use of larger sample sizes is recommended in order to maintain an acceptable level of consumer protection. The choice of a suitable sampling plan will be governed by cost considerations. Larger sample sizes will give better discrimination but at increased cost. Purchasers may, for example, rely upon their experience with a particular supplier when assessing the sample sizes to use for small numbers of lots.

The sampling plans given in Table B.1, normal inspection, when applied to isolated lots, provide approximately the same level of consumer protection as those given in Annex A when used in conjunction with the switching rules. Attention is drawn to the possibility of using double or multiple sampling plans which might reduce the total number of female condoms that need to be tested to demonstrate conformity when quality is significantly better than the AQLs.

The producers' and consumers' risk associated with these sampling plans can be obtained by reference to the relevant tables and operating characteristic curves given in ISO 2859-1.

NOTE There is no simple mathematical relationship between the sample size and the lot size. Increasing sample sizes independently of the lot size permits a more reliable estimate of lot quality to be made.

Table B.1 — Sampling plans and acceptance criteria for isolated lots

Attributes	Inspection level[a]	Acceptance criteria
Dimensions (including retention feature dimensions)	13 female condoms	All samples should fall within the manufacturer's specified limits.
Bursting volume and pressure	General inspection level I but at least code letter L	AQL of 1,5
Individual container integrity	Special inspection level S3 but at least code letter H	AQL of 2,5
Freedom from holes	General inspection level I but at least code letter N	AQL of 0,25
Visible defects	General inspection level I but at least code letter N	AQL of 0,4
Packaging and labelling	13 consumer packages and 13 individual containers	All should conform
Quantity of lubricant	13 female condoms	All should conform
Retention feature properties	Special inspection level S-2	AQL of 2,5

[a] See ISO 2859-1 where relevant.

Applications for these sampling plans include the following:

a) type testing as part of a certification procedure;

b) cases where the total number of lots being assessed is insufficient to allow the switching rules to be effective;

c) in cases of dispute involving isolated lots, e.g. for referee testing.

Annex C
(normative)

Determination of lubricant mass for individual female condom containers

C.1 Principle

The lubricant mass is determined by weighing the packaged female condom, removing the lubricant from the female condom, retention and insertion features and individual container by washing with a solvent, reweighing the female condom, retention and insertion features and individual container and calculating the lubricant mass removed during washing.

C.2 Apparatus

C.2.1 **Ultrasonic cleaning bath(s) or suitable container**, e.g. beaker and stirrer.

C.2.2 **Balance**, accurate to 1 mg.

C.2.3 **Solvent**, **propan-2-ol** or other suitable cleaning solvent, or aqueous surfactant solution of laboratory reagent grade depending on the material(s) used in the female condom. Alternative solvents or aqueous surfactant solutions may be specified by the manufacturer providing the choice of alternative solvent is justified and the test procedure has been adequately validated. The manufacturer may use alternative methods of removing the lubricant other than washing with solvent subject to satisfactory validation studies. Full details of the method shall be included in the data sheet for the product and copies of appropriate validation reports shall be provided to interested parties on request.

C.3 Procedure

C.3.1 Weigh each individual closed female condom container to the nearest 1 mg and record the results (m_1).

C.3.2 Cut the individual container carefully around three edges and remove the undamaged female condom.

C.3.3 Remove any retention or insertion features that are not permanently attached to the female condom.

C.3.4 Unfold or unfurl the female condom and then cut up one side using scissors. Wipe the female condom, the removed retention and insertion features and the individual container free of lubricant as much as possible.

C.3.5 When using the ultrasonic bath: immerse the female condom, remove retention and insertion features and individual container in the solvent in an ultrasonic bath and wash for 2 min to 10 min. Repeat washing in clean solvent as many times as necessary to achieve constant mass after two successive washes (within 10 mg), after drying as in C.3.7 to C.3.8.

C.3.6 When washing the female condoms manually: immerse the female condom, remove retention and insertion features and individual container in the solvent in a bath and wash with manual agitation.

Repeat washing in clean solvent as many times as necessary to achieve constant mass after two successive washes (within 10 mg), after drying as in C.3.7 to C.3.8.

C.3.7 Remove the female condom and individual container from the solvent and wipe to remove excess solvent.

C.3.8 Dry the female condom and individual container to constant mass (within 10 mg) at a temperature not exceeding 50 °C.

C.3.9 Weigh each dry female condom, remove retention and insertion features and individual container to the nearest 1 mg (m_2).

C.3.10 The total quantity of lubricant for the individually packaged female condom (m_{tot}) is obtained by subtracting the mass of the female condom, removed retention and insertion features and package (m_2) from the total mass of the packaged female condom (m_1).

$$m_{tot} = m_1 - m_2 \quad \text{(C.1)}$$

C.4 Expression of results

Report the average amount of lubricant recovered to the nearest 10 mg, the maximum and minimum values obtained and the number of results non-conforming with the specification.

Annex D
(normative)

Determination of female condom length

D.1 Principle

The unpackaged female condom is allowed to hang freely over a graduated mandrel and its length is observed and recorded.

D.2 Apparatus

D.2.1 **Mandrel**, with a scale divided into millimetres. As each design of a female condom can have a unique geometry, the mandrel dimensions that will support the closed end of the female condom without distorting the shape of the female condom shall be specified. This information shall be included in the data sheet. The mandrel shall have a hemispherical tip. The recommended diameter for the hemispherical tip is 25 mm but this may be adjusted to suit a specific design of female condom. The closed end of the female condom shall fit snuggly on the tip of the mandrel. The length scale on the mandrel shall begin with zero at the tip of the closed end of the female condom.

The mandrel may optionally be fitted with a device such as a plate or an arm to reduce parallax error when measuring the length of the female condom.

D.3 Procedure

D.3.1 Move the female condom inside the individual container so that it is away from the area where the package is to be torn. Tear the container and remove the female condom.

Scissors or other sharp instruments shall not be used to open the individual container.

D.3.2 Unfold or unfurl the female condoms, remove any insertion devices and internal retention features that are not permanently attached to the female condom and might interfere with the measurement. Smooth out any wrinkles caused by the female condoms having been stored in the individual container. Do not remove any external retention features. Lubricants may be removed and suitable powders may be added to avoid sticking. Do not stretch the female condom.

D.3.3 Put the female condom over the mandrel and let it hang freely, stretched only by its own mass.

D.3.4 Measure, to the nearest millimetre, the length of the female condom on the scale at the open end. If the measurement varies along the circumference, use the shortest measurement read.

D.3.5 Female condoms subjected to this test may also be used for the determination of width.

D.4 Expression of results

Report the length of each tested female condom to the nearest millimetre.

Annex E
(normative)

Determination of female condom width

E.1 Principle

The unpackaged female condom is allowed to hang freely over the edge of a ruler and its width is observed and recorded.

E.2 Apparatus

E.2.1 **Ruler**, with a scale divided into millimetres.

E.3 Procedure

E.3.1 Move the female condom inside the individual container so that it is away from the area where the container is to be torn. Tear the container and remove the female condom.

Scissors or other sharp instruments shall not be used to open the individual container.

E.3.2 Unpack the female condom. Remove any internal retention feature or insertion feature that is not permanently attached to the female condom to allow the female condom to lay flat. If a lubricated female condom does not hang freely, then the lubricant shall be removed and suitable powders may be added to avoid sticking. To facilitate measuring, mark three positions on the female condom that are 25 %, 50 % and 75 % along the length of the female condom from the closed end (use the manufacturer's specified nominal length to determine these points) or mark at the positions specified by the manufacturer if these are different. Lay the female condom flat over the edge of the ruler, perpendicular to the female condom's axis, allowing it to hang freely.

E.3.3 Measure the width of the female condom at positions 25 %, 50 % and 75 % along the length of the female condom from the closed end to the nearest 1,0 mm (use the manufacturer's specified nominal length to determine these points) or at the positions specified by the manufacturer if these are different.

E.3.4 Female condoms subjected to this test may also be used for determining the length.

E.4 Expression of results

Report the width of each tested female condom, at each point along the length of the female condom to the nearest millimetre.

Annex F
(normative)

Determination of female condom thickness

F.1 Principle

The female condom is cut open and laid flat. The thickness of the female condom is measured at three different positions along the length of the female condom (25 %, 50 % and 75 % from the closed end). At each of these positions, three measurements are made at equidistant points around the circumference of the female condom.

F.2 Apparatus

F.2.1 **A flat footed micrometer**, dial or digital type, with measurement intervals not larger than 0,001 mm, with foot diameter in the range 3 mm to 10 mm, with a foot pressure (22 ± 5) kPa, and with the foot parallel to a flat base plate.

F.2.2 **Scissors or blade**, for cutting female condoms open.

F.3 Procedure

F.3.1 Move the female condom inside the unopened individual container so that it is away from the area where the container is to be torn. Tear the container and remove the female condom.

F.3.2 Remove any insertion devices and internal retention features that are not permanently attached to the female condom and unfurl or unfold the female condom, ensuring that it is not excessively stretched in any direction.

F.3.3 To facilitate measuring, mark the female condom at positions that are 25 %, 50 % and 75 % along the length of the female condom from the closed end (use the manufacturer's specified nominal length to determine these points) or at the positions specified by the manufacturer if these are different.

F.3.4 Cut the female condom open longitudinally using scissors or a suitable blade.

F.3.5 Wash the female condom in propan-2-ol or other suitable solvent or wipe the female condom to remove the lubricant. If a solvent is used to remove the lubricant, ensure that the female condom is adequately dried before proceeding.

F.3.6 Zero the gauge and unless specified differently by the manufacturer, measure the thickness of the female condom at a position that is 25 % along the length of the female condom from the closed end (use the manufacturer's specified nominal length to determine these points). Repeat measurements at two more points that are equidistant from each other around the circumference of the female condom in this position. The spacing of these points should be chosen so that the three measurement locations are equidistant from one another around the circumference if the female condom were uncut.

F.3.7 Repeat step F.3.6 at two more positions that are 50 % and 75 % along the length of the female condom from the closed end (use the manufacturer's specified nominal length to determine these points) or at the positions specified by the manufacturer.

F.3.8 Repeat steps F.3.1 to F.3.6 for the remaining female condom samples.

F.4 Expression of results

Report to the nearest 0,001 mm the average thickness at each of the three points tested for each female condom.

Annex G
(normative)

Testing for female condom individual container integrity

G.1 General

Individual container integrity refers to the possibility of breaches in sealed individual female condom containers that might result in the leakage of lubricant. Such breaches will also allow oxygen to enter the container.

Given the wide range of packaging options that can be used for female condoms, it is not possible to specify a test method that is suitable for all individual container types. The following test method is based on that used for male latex condoms and is recommended as the method that should be used by default. It might be necessary to modify the pressure to adapt the test for some packaging types. If the method is changed or another method is used, then full details of the test method shall be provided in the data sheet.

The test given in this annex cannot detect leakage due to micro-porosity or gas permeability of the materials used to construct the individual containers.

Individual container integrity shall be measured in accordance with the following test method using a vacuum of (20 ± 5) kPa absolute pressure.

Some leaks might not be detected by this procedure. Positive pressure inside the female condom container after the vacuum is drawn might force the lubricant, if present, to plug small leaks. The size of the leak that can be detected is dependent upon the lubricant and the nature of the packaging material.

G.2 Test method

G.2.1 Apparatus

G.2.1.1 Vacuum chamber, capable of withstanding approximately one atmosphere pressure differential, fitted with a vacuum-pump, a vacuum gauge and the possibility to inspect the interior during the test.

G.2.2 Reagents

G.2.2.1 Immersion fluid, water, optionally with a dye added to assist in detecting any water leaking into the individual containers.

G.2.3 Test specimen

Female condoms in their individual containers.

G.2.4 Conditioning

The test sample and test fluid shall be at equilibrium with normal room temperature (15 °C to 35 °C).

G.2.5 Procedure

Submerge the individual containers in water contained in the vessel within the vacuum chamber. The uppermost surface of the containers shall be covered by not less than 25 mm of water. If a dye is added to the water, leakage of water into the container will be easier to detect.

Two or more containers may be tested at the same time, provided that they are placed in such a manner that all parts of every container under test can be observed for leakage during the test.

Evacuate the chamber to an absolute pressure of (20 ± 5) kPa. Observe the containers throughout the test for leakage in the form of a steady progression of bubbles coming from the individual containers. Isolated bubbles caused by entrapped air are not considered as leaks. Flexible packaging with little or no headspace cannot be reliably evaluated with this test method.

Hold vacuum for 1 min. Release the vacuum, remove the lid and examine the containers for the presence of water inside.

G.2.6 Interpretation of results

If there are bubbles indicating leaks in a container as the vacuum increases or when held at specified vacuum, then specimen fails the tests.

If the test fluid is visible inside a container, the container fails the test.

If there are no bubbles observed indicating leaks and if no test fluid is visible inside a container, the container passes the test.

G.2.7 Test report

When the test is complete, record the numbers of containers with detected leaks.

Annex H
(normative)

Determination of barrier properties using the bacteriophage method

H.1 General

This annex provides the rationale, methodology and the required sensitivity to test the ability of a female condom to act as a barrier to transmission of sexually transmitted infections (STIs), including viruses.

A female condom is a medical device designed to be used by a woman to prevent pregnancy and transmission of STIs during sexual intercourse. In order to make a claim that a female condom is effective against STIs, appropriate laboratory tests shall be performed. Since viruses are the smallest aetiological STI agents, the challenge particle should be a small virus or virus-size particle. The challenge particle, solution properties, test pressure and test duration should be chosen to simulate, as closely as possible, real-use conditions. Choices of parameters that make the *in vitro* test more stringent than expected real-use conditions are encouraged, with appropriate justification. However, movement of the female condom during the test is not required.

The choice of a challenge particle has several important aspects. Signal-to-noise ratio should be considered. A biological assay might be preferred in general because the expected background "noise" signal of a biological assay is less than that of an assay using radioactive or other labelled viruses or virus-like particles.

In order for the test to be used to demonstrate safety with regard to STI barrier properties, the test virus shall be smaller than hepatitis B virus (42 nm diameter), the smallest aetiological agent for an STI. Surrogate viruses such as bacterial viruses (bacteriophages) of appropriate size and shape may be substituted for human pathogens. This protocol suggests use of a small bacteriophage as challenge particle because bacteriophage assays are safe, fast and comparatively less expensive than alternate assays. Additionally, bacteriophages can be readily obtained at sufficient titre to provide an adequate challenge concentration. The bacteriophage, Phi-X174, should be considered as the challenge virus. Other similar challenge bacteriophages may be used, but shall be justified as equivalent to bacteriophage, Phi-X174.

H.2 Principle

The test consists of filling the female condom with a virus-containing buffer and determining whether any viruses penetrate the female condom barrier during submersion in a collection buffer. Virus penetration is quantified and reported as the equivalent volume of penetrating challenge buffer needed to account for the amount of virus penetration into the collection buffer. Positive control experiments of the same duration are needed to ensure that the overall test is functioning properly.

H.3 Buffer solutions

H.3.1 The challenge buffer solution and the collection buffer solution shall have a pH value of approximately 7,0.

H.3.2 The challenge buffer solution and the collection buffer solution shall have a salinity of any one of the several variations of physiological saline.

H.3.3 The challenge buffer solution and the collection buffer solution shall have a surface tension less than 0,05 N/m.

H.3.4 The challenge buffer solution shall contain the challenge virus at adequate titre at the beginning of the test so that even at the end of the test, the titre is sufficient. Sufficient titre for a small, approximately spherical virus is at least 10^8 plaque-forming units/ml.

NOTE One adequate buffer is 0,1 % Triton X-100[1)]. Physiological saline has a lower viscosity than semen and therefore, provides a more stringent test. Using saline therefore permits the test to be performed at room temperature (25 + 2) °C.

H.4 Apparatus

H.4.1 The apparatus shall provide a leak-proof seal at the female condom open end and leave an appropriate length of test portion available for the virus penetration test.

H.4.2 The apparatus shall restrain the female condom to prevent over expansion under pressure. Dimensions of the restraining device should allow expansion of the test portion of the female condom to a length greater than the length of the test female condom and a circumference appropriate for the female condom material tested. The contour of the restraining device should approximate that of the female condom. Strainers of the same size and material should be used with the test female condoms and with the comparative female condoms.

H.4.3 The apparatus shall provide for exposure of the inside of the female condom to aqueous challenge virus suspension.

H.4.4 The apparatus shall provide for application of pressure to that suspension.

H.4.5 The apparatus shall allow for submersion of the test portion of the female condom in collection fluid.

H.4.6 The apparatus shall provide for access to the challenge virus suspension inside the female condom for assay following the test.

H.5 Sample size

Use a minimum of 60 female condoms, 20 condoms from each of the three lots, in order to determine acceptability.

A comparator condom should be used to assist in the interpretation of the results. The comparator condom may be a natural rubber latex male condom that conforms to ISO 4074 or the comparative condom to be used in the clinical study. The comparator condom is to be tested as a control using steps H.3.1 to H.3.4.

H.6 Preparation of test samples

H.6.1 Handle test female condoms carefully so they are not damaged during the test procedure.

H.6.2 Wear gloves as a precautionary measure to prevent abrasion or puncture by fingernails, rings, etc.

1) Triton X-100 is the trademark of a product supplied by Sigma-Aldrich. This information is given for the convenience of users of this document and does not constitute an endorsement by ISO of the product named. Equivalent products may be used if they can be shown to lead to the same results.

H.6.3 Remove any retention and insertion features that are not affixed to the female condom.

H.6.4 Remove accompanying lubricants and/or spermicides, if present, to prevent interference with the test. Wash and dry the female condom in accordance with steps C.3.5 to C.3.8 to constant mass, ±10 mg without damaging the female condom material.

H.7 Procedure

H.7.1 Fill the female condom with the challenge buffer.

H.7.2 Apply pressure to the internal volume of the female condom so that the pressure of the challenge fluid is equivalent to 8 000 Pa.

H.7.3 Place the female condom in a collection container with sufficient buffer to allow fluid contact with the test surface of the female condom and to collect any virus that penetrates through the female condom.

H.7.4 Submerge the filled, pressurized female condom in the collection buffer for at least 30 min.

H.7.5 Mix the collection fluid just prior to assaying so that the assay aliquots are representative.

H.7.6 Assay the collection buffer for the challenge virus to determine whether any virus has penetrated the female condom and passed into the collection buffer.

H.7.7 Calculate the equivalent volume of challenge virus penetration needed to account for the amount of virus found in the collection buffer.

H.8 Positive control testing

Use positive controls that meet the following requirements.

a) Follow the same procedures in H.6 and H.7 using female condoms with representative pinholes placed using a small gauge needle, approximately 30 µm diameter, laser or other suitable method. Female condoms with intentional pinholes may be used, although it is recognized that it is difficult to produce small pinholes.

b) Verify the stability of virus concentration. Determine whether the challenge virus remained at a stable concentration in the female condom during the test. Data from several positive control female condoms shall be collected as part of each female condom test. The titre of the challenge virus suspension inside the female condom at the end of the test is compared to the titre originally placed in the female condom. This determines if and how much the challenge virus titre changes during the test because of interaction with the female condom and the test apparatus or other factors.

c) Verify detectability. Determine whether any virus that penetrates the female condom remains detectable in the collection buffer over the test period. This may be done by "spiking" the collection buffer with a low concentration of challenge virus before a mock test (where there is no virus inside the female condom and for the same duration) and assaying the titre of the collection buffer at the beginning and end of the mock test. This determines if and how much the penetrated virus titre changes during the test as a result of interaction with the outside of the female condom, the restrainer or the collection container.

d) Increase the starting titre of the challenge virus if the stability controls or the detection controls (or both) indicates the loss of virus titre below 10^8 plaque-forming units/ml to compensate for the loss and to maintain the overall sensitivity of the test.

e) It might be useful to determine via controls (e.g. settle plates) whether contamination caused by aerosolized virus or other leaks might lead to false evidence of virus penetration of the female condom.

H.9 Detection limits and reporting

H.9.1 Detection limit explanation

H.9.1.1 For 95 % confidence that an assay will find at least one virus when virus is present [i.e. P(0) < 0,05], the average number of infectious particles per total volume assayed shall be at least three; e.g. there is 95 % probability that a titre of 1 pfu/ml will result in at least one plaque in a 3 ml total assay. Thus, the sensitivity or detection limit of this assay can be claimed as 1 pfu/ml when 3 ml is assayed.

H.9.1.2 Detection limit expressed as volume of challenge virus suspension that penetrated the barrier is probably the most useful measure of test sensitivity. For example, in a real-life risk assessment, the volume of transmitted virus-containing fluid can be translated into infectious units when the titre of a pathogenic virus (in real life) is known.

H.9.1.3 The test procedure shall be able to detect 2×10^{-6} ml penetration of the challenge virus suspension. This may be done by:

a) using a challenge buffer titre of 1×10^{8} pfu/ml;

b) using a collection buffer volume of 200 ml;

c) assaying 1 ml in triplicate from the collection buffer (assuming no loss of virus titre in the challenge buffer nor in the collection buffer): the assay detection limit of 1 pfu/ml is equivalent to penetration by 200 pfu (1 pfu/ml × 200 ml) or 2×10^{-6} ml (200 pfu divided by 1×10^{8} pfu/ml).

H.9.2 Detection limit analysis

H.9.2.1 Assay at least 1 ml in triplicate (3 ml total).

H.9.2.2 Present the individual results for each female condom sample tested in a table that includes:

a) the challenge buffer virus titre;

b) the virus titre in the collection buffer;

c) any correction factor for loss of virus (determined in the controls);

d) the calculated challenge volume that penetrated (for the female condoms that allowed virus transmission). If some loss of virus titre occurs either inside the female condom or outside in the collection container, the calculation should include the appropriate correction for such loss. For female condoms that apparently did not allow virus transmission, the detection limit of that particular test should be given, e.g. as 2×10^{-6} ml.

H.9.3 Test report

H.9.3.1 Positive control

Reporting the results of the positive control experiment should be done using the same reporting format as with virus penetration of test samples in H.9.3.3.

H.9.3.2 Challenge virus stability

Results from the test of challenge virus stability should be presented in tabular form, where the data for each female condom are individually reported. The following information for each test sample shall be reported:

a) date when the test was performed;

b) titre of challenge buffer placed inside the female condom at the beginning of the test;

c) titre of challenge buffer inside the female condom at the end of the test;

d) calculated ratio of final to beginning titre.

H.9.3.3 Challenge to virus detection

Results from tests to determine the detection of penetrated virus should be in tabular form, where the data for each female condom are individually reported. The following information for each test sample shall be reported:

a) date when the test was performed;

b) titre of collection buffer at the beginning of the test;

c) titre of collection buffer at the end of the test;

d) calculated ratio of final titre to titre at the beginning of the test.

Annex I
(informative)

Determination of microbial contamination

I.1 General

This annex gives three methods for determining microbial contamination (bioburden) on female condoms. Although these methods have been shown to work effectively with male and female condoms, any methods used need to be validated by the user.

The first method allows the total viable count to be estimated on a female condom. The second method allows the total viable count to be determined but also allows the specified organisms to be identified. The third is based on methods described in the European Pharmacopoeia for counting the total number of viable, aerobic bacteria on agar plates (direct plating method).

These methods, which are given as examples, are known to work with male and female condoms. Other methods may be used. Methods for determining microbial contamination on sterile medical devices are given in ISO 11737-1.

Residual compounding ingredients in female condoms made from latex (natural and synthetic) can inhibit bacterial growth and interfere with the assays. It is recommended that culture media used contain additives, such as lecithin and polysorbate (e.g. Tween 80®[2]), that will neutralize these antimicrobial effects. It is essential that the amounts of lecithin and polysorbate (e.g. Tween 80®[2]) used are validated with any specific female condom type to ensure that any residual inhibitory effects from the female condom are neutralized without any direct inhibitory action on bacterial growth due to the additives themselves. Methods for validating test methods are given in ISO 11737-1:2006, Annex C. Routine confirmatory testing using spiked samples is strongly recommended, for example, using the methods described in United States Pharmacopeia USP 37 <62>. Further information on determining the effectiveness of the culture medium and the validity of the counting method is given in I.4.3.

The complete female condom including the internal and external features should be evaluated for microbial contamination. To facilitate extraction, it might be necessary to cut up the retention features and/or evaluate them separately. If the retention features are evaluated separately, then it is necessary to add any counts found on these components to the sheath counts in order to get the total counts for the complete female condom. The same applies to any insertion feature included with the female condom. It might be necessary to adjust the volume of extraction medium to ensure competed coverage of all the components of the female condom during the extraction procedure. If so, then it is essential to use the correct dilution factor when calculating the counts on the female condom.

It is recommended that a preliminary identification of any organisms found is conducted irrespective of the test method used for enumeration. Running tests in parallel using selective media assists preliminary identification. A gram stain, coagulase test and oxidase test will indicate whether species identification is required. Biochemical profiles may be used to identify organisms to species level.

I.2 Enumeration of total population of aerobic microorganisms on foiled female condoms

I.2.1 A random sample of 10 to 13 female condoms should be taken from the lot. Each female condom is tested individually.

2) Tween 80® is the trademark of a product supplied by Sigma-Aldrich. This information is given for the convenience of users of this document and does not constitute an endorsement by ISO of the product named. Equivalent products may be used if they can be shown to lead to the same results.

I.2.2 Using sterile forceps and scissors, aseptically remove a female condom from the individual container and unfold or unfurl the female condom. If necessary, remove any external, insertion and internal retention features that are not permanently attached to the female condom. Cut the female condom to allow it to be opened out and also cut the internal and external retention features and any insertion feature into suitable sized pieces to permit extraction. Place all the pieces into the minimum quantity of peptone water containing 0,3 % lecithin and 3 % polysorbate (e.g. Tween 80®[2]) to cover the female condom and retention/insertion features. It might be necessary to extract the retention/insertion features separately depending upon the design of the female condom. Lecithin and polysorbate are added to neutralize any residual inhibitory effects from the female condoms. It is essential that the amount of lecithin and polysorbate (e.g. Tween 80®[2]) used is validated with any specific condom type to ensure that any residual inhibitory effects from the female condom are neutralized without any direct inhibitory action on bacterial growth due to the additives themselves. Letheen broth may be used as an alternative extraction medium.

I.2.3 In order to remove the bioburden from the female condom and retention/insertion features, mix the contents with a shaker, stomacher or vortex mixer for the time previously determined from validation studies. Care should be taken not to mix too vigorously as this might kill some microbes.

I.2.4 Using a sterile pipette, transfer 1 cm^3 of the extraction fluid into 20 cm^3 of molten Sabourauds Dextrose Agar (SDA) kept at 40 °C. Mix gently to disperse the sample throughout the media and pour into a sterile Petri dish. Allow to set.

I.2.5 Repeat with another SDA and with 2 × 20 cm^3 of Tryptone Soya Agar (TSA).

I.2.6 Repeat extractions run in parallel using selective media assist identification of any organisms found. This is particularly useful for demonstrating the absence of the organisms listed in Clause 10 (*Staphylococcus aureus, Pseudomonas aeruginosa* and *Enterobacteriaceae,* including *Escherichia coli).*

I.2.7 Incubate the SDA plates at 20 °C for five days and incubate TSA plates at 30 °C for three days.

I.2.8 Inspect the TSA plates at three days and count colonies. Re-incubate and count at five days.

I.2.9 Count the number of colonies on each TSA plate and find the average of the two counts. Examine the SDA plates and count fungal and yeast colonies. Calculate the average count as above. Make corrections for dilution and recovery factors (previously determined by the validation tests).

NOTE The total viable aerobic count is determined by adding together the corrected averages of the fungal and bacterial counts (SAB and TSA).

I.2.10 Some identification of bacteria is required in order to confirm the absence of the specified organisms. Gram stain and colonial morphology will identify gram positive cocci and gram negative bacilli. A positive coagulase test will indicate probable *Staphylococcus aureus*, while the oxidase test will indicate possible *Pseudomonas* species. Results from these short tests will determine if further identification is required. Biochemical profiling will identify organisms to species level.

I.3 Enumeration of total viable aerobic microbial population and tests for specified microorganisms on foiled female condoms

I.3.1 This test is conducted on a pooled sample of 13 female condoms. The samples should be taken randomly from a single lot.

I.3.2 Using the aseptic technique, remove 13 female condoms from the individual containers with sterile forceps into a large sterile dish. If necessary remove any removable internal and external retention

features and any insertion feature. Cut up the female condoms and retention/insertion features using sterile scissors.

I.3.3 Weigh 100 g of material and place it in 1 000 cm^3 of extraction media in either a suitably sized bottle or a stomacher bag. The extraction media should be capable of neutralizing any residual antimicrobial effect from the female condoms. Suggested media is peptone water with the addition of 3 % polysorbate (e.g. Tween 80®[2]) and 0,3 % lecithin. The lecithin and polysorbate (e.g. Tween 80®[2]) are added to neutralize any residual inhibitory effect of the female condom; the amounts used need to be validated for any specific female condom type to ensure that any residual inhibitory effects from the female condom are neutralized without any direct inhibitory effect due to the additives themselves.

I.3.4 Stomach or mix the sample for the time required to remove the bioburden, as previously determined by validation testing.

I.3.5 Using a sterile pipette, transfer 10 cm^3 of the female condom extraction fluid into 100 cm^3 of soya casein digest broth and gently mix.

I.3.6 Proceed using the methods described in USP 37 Microbiological tests <61> and <62> or in the German Pharmacopoeia (DAB) V2.1.8.1 and V.2.1.8.2 in order to determine total viable count of bacteria and fungi and absence of *Escherichia coli, Staphylococcus aureus* and *Pseudomonas aeruginosa*.

I.4 Enumeration of the total viable aerobic bacteria and fungi on Agar plates (direct plating method) according to the methods in the European Pharmacopoeia

I.4.1 Preparation of the sample

Unless otherwise prescribed, use a sample of 13 female condoms. Select the female condoms at random from the bulk material or from the available containers of the preparation under aseptic conditions. If necessary, to obtain the required quantity, mix the contents of a sufficient number of containers to provide each sample. The female condoms should be handled using aseptic procedures and conditions.

Cut the female condoms and retention/insertion features using sterile scissors into small pieces. Take a sample of the cut female condoms and insertion/retention features with a total weight of (100 ± 1) g and shake for (5 to 10) min on a mechanical rocker at approximately 1 000 rpm in 1 000 cm^3 of a suitable medium [e.g. sodium chloride peptone buffer solution (pH 7,0)] with the addition of glass beads. The extraction medium should not have any antimicrobial properties. If necessary, add a suitable surface-active agent such as 1 g/cm^3 of polysorbate 80 to assist the suspension of poorly wettable substances. If the female condoms are known to have antimicrobial activity, a neutralizing agent may be added to the diluent. Suitable neutralizing materials are polysorbate and lecithin. The types and amounts of neutralizing additives need to be validated. If necessary, adjust the pH to about pH 7 and prepare further serial tenfold dilutions using the same diluent.

I.4.2 Examination of the sample

I.4.2.1 Membrane filtration

Use membrane filters having a nominal pore size not greater than 0,45 µm and whose effectiveness to retain bacteria has been established. The type of filter material is chosen in such a way that the bacteria retaining efficiency is not affected by the components of the sample to be investigated. Cellulose nitrate filters, for example, may be used for aqueous, oily and weakly alcoholic solutions and cellulose acetate filters, for example, for strongly alcoholic solutions. The filtration apparatus is designed to allow the transfer of the filter to the culture medium.

Transfer a suitable amount of the sample prepared as described (preferably representing 10 g of the product or less if large numbers of colony-forming units are expected) to each of two membrane filters and filter immediately. Wash each filter with three quantities, each of about 100 cm^3 of a suitable liquid

such as buffered sodium chloride-peptone solution pH 7,0. To this solution, surface-active agents such as polysorbate 80, or inactivators of antimicrobial agents may be added. If validated, less than three washes may be applied. Transfer one of the membrane filters, intended primarily for the enumeration of bacteria, to the surface of a suitable agar medium, such as medium B and the other, intended primarily for the enumeration of fungi, to the surface of a suitable agar medium, such as medium C. Incubate the plate of agar medium B at 30 °C to 35 °C and the plate of agar medium C at 20 °C to 25 °C for five days, unless a reliable count is obtained in a shorter time. Select plates with the highest number less than 100 colonies and calculate the number of colony-forming units per gram or millilitre of product. Place one membrane onto agar medium B for total aerobic microbial count, the other membrane onto agar medium C for the count of fungi. The total viable aerobic count is the sum of the bacterial and fungal counts.

I.4.2.2 Plate-count methods

I.4.2.2.1 Pour-plate method

Using Petri dishes 9 cm in diameter, add to each dish 1 cm^3 of the sample prepared as described in I.4.1 and 15 cm^3 to 20 cm^3 of a liquefied agar medium suitable for the cultivation of bacteria (such as medium B) or 15 cm^3 to 20 cm^3 of a liquefied agar medium suitable for the cultivation of fungi (such as medium C) at not more than 45 °C. If larger Petri dishes are used, the amount of agar is increased accordingly. Prepare for each medium at least two Petri dishes for each level of dilution. Incubate the plates at 30 °C to 35 °C (20 °C to 25 °C for fungi) for 5 days, unless a reliable count is obtained in a shorter time. Select the plates corresponding to one dilution and showing the highest number of colonies less than 300 (100 colonies for fungi). Take the arithmetic average of the counts and calculate the number of colony-forming units per gram or millilitre.

I.4.2.2.2 Surface-spread method

Using Petri dishes 9 cm in diameter, add 15 cm^3 to 20 cm^3 of a liquefied agar medium suitable for the cultivation of bacteria (such as medium B) or a liquefied agar medium suitable for the cultivation of fungi (such as medium C) at about 45 °C to each Petri dish and allow to solidify. If larger Petri dishes are used, the volume of the agar is increased accordingly. Dry the plates, for example, in a LAF bench or in an incubator. Spread a measured volume of not less than 0,1 cm^3 of the sample prepared as described in I.4.1, over the surface of the medium. Use at least two Petri dishes for each medium and each level of dilution. For incubation and calculation of the number of colony-forming units, proceed as described for the pour-plate method.

I.4.3 Effectiveness of culture media and validity of the counting method

Grow the bacterial test strains separately in containers containing a suitable liquid medium (such as broth medium A) at 30 °C to 35 °C for 18 h to 24 h. Grow the fungal test strains separately on a suitable agar medium (such as medium C without antibiotics) at 20 °C to 25 °C for 48 h for *Candida albicans* and at 20 °C to 25 °C for 7 days for *Aspergillus niger*.

Suitable test strains for assessing the effectiveness of the culture media and validity of the counting method include:

— *Staphylococcus aureus* such as ATCC 6538 (NCIMB 9518, CIP 4.83);

— *Escherichia coli* such as ATCC 8739 (NCIMB 8545, CIP 53.126);

— *Bacillus subtilis* such as ATCC 6633 (NCIMB 8054, CIP 52.62);

— *Candida albicans* such as ATCC 10231 (NCPF 3179, IP 48.72);

— *Aspergillus niger* such as ATCC 16404 (IMI 149007, IP 1431.83).

Use buffered sodium chloride-peptone solution pH 7,0 to make reference suspensions containing about 100 colony-forming units per millilitre. The actual count should be confirmed using a suitable reference method. Any neutralizing agent or other additives used in the female condom assay should be included

in the microorganism suspensions. Use the suspension of each of the microorganisms separately as a control of the counting methods, in the presence and absence of the product to be examined. When testing the membrane filtration method or the plate-count method, a count of any of the test organisms differing by not more than a factor of five from the calculated value from the inoculum is to be obtained. When testing the most-probable-number method, the calculated value from the inoculum is to be within the 95 % confidence limits of the results obtained. To test the sterility of the medium and of the diluent and the aseptic performance of the test, carry out the method using sterile sodium chloride-peptone solution pH 7,0 as the test preparation. There should be no growth of microorganisms.

The solutions and culture mediums recommended are described in the Chapter 2.6.13 of European Pharmacopoeia.

I.4.4 Interpretation of the results

The bacterial count will be considered to be equal to the average number of colony-forming units found on agar medium B. The fungal count will be considered to be equal to the average number of colony-forming units on agar medium C. The total viable aerobic count is the sum of the bacterial count and the fungal count as described above. If there is evidence that the same types of microorganisms grow on both media, this may be corrected. If the count is carried out by the most probable-number method, the calculated value is the bacterial count. Calculate the total viable aerobic count separately for each of the five samples.

I.4.5 Identification

Some identification of bacteria is required in order to confirm the absence of the organisms specified in Clause 10 (*Staphylococcus aureus, Pseudomonas aeruginosa* and *Enterobacteriaceae,* including *Escherichia coli)*. Gram stain and colonial morphology will identify gram positive cocci and gram negative bacilli. A positive coagulase test will indicate probable *Staphylococcus aureus*, while the oxidase test will indicate possible *Pseudomonas* species. Running simultaneous extractions using selective media assists identification. Results from these short tests will determine if further identification is required. Biochemical profiling will identify organisms to species level.

I.5 Expression of results

Report the results from each test including the total counts, fungal and bacterial counts where these are determined separately and the identity of any organisms identified by the tests.

Annex J
(normative)

Determination of bursting volume and bursting pressure

J.1 Principle

A specified length of the female condom is inflated with air and the volume and pressure required to burst the female condom are measured and recorded.

J.2 Apparatus

J.2.1 Inflation apparatus, suitable for inflating the female condom with clean, oil-free and moisture free air at a specified rate, provided with equipment for measuring air volume and pressure and having the following features:

a) a pressure sensor configured so that there is no pressure differential between the female condom and the pressure sensor;

b) an apparatus for recording the volume of inflation air, configured so that there is no pressure differential between the measuring device and the female condom, thereby ensuring that the volume of the air is measured or calculated at the appropriate pressure within the female condom and not at the line pressure which might be higher;

c) a rod or mandrel with a smooth spherical or hemispherical head 20 mm in diameter to ensure that the female condom is correctly mounted at the correct inflation length. The inflation length shall be specified by the manufacturer and, as far as is reasonable and practicable, be at least 90 % of the nominal length of the female condom;

d) pressure and volume measuring equipment capable of:

   1) a maximum permissible limit of error of ±3 % for volumes greater than 10 dm^3, whatever method is used to measure the volume, and

   2) measuring the pressure at burst of the female condom with a maximum permissible limit of error of ±0,05 kPa.

The female condom manufacturer is responsible for providing any specifications or requirements for the inflation apparatus that are specific to its female condom design.

J.2.2 Clamping apparatus, for example, a clamping ring, having no sharp edges or protrusions.

The female condom manufacturer is responsible for providing any specifications or requirements for the clamping apparatus that are unique to its specific female condom design. The recommended material of construction for the clamping apparatus is non-brittle, transparent plastic. The clamping apparatus should not stretch the female condom as it clamps the condom. It should clamp the sheath close to the external retention feature. Alternatively, if the design of the female condom permits, the external retention feature should be clamped directly (this is the preferred method of clamping). The clamping device shall be of sufficient diameter to prevent creasing and rucking of the female condom. A minimum diameter of 50 mm is recommended.

J.2.3 Inflation cabinet, having a facility for viewing the female condom during inflation and of sufficient size to allow the female condom to expand freely without touching any part of the cabinet.

J.3 Procedure

J.3.1 It is recommended that suitable gloves or finger cots be worn while handling the female condom. In cases of dispute, gloves shall be worn.

J.3.2 Move the female condom inside the individual container so that it is away from the area where the container is to be torn. Tear the container and remove the female condom. Scissors or other sharp instruments shall not be used to open the individual container.

J.3.3 Remove any internal retention feature and/or insertion device that is not permanently attached to the female condom. The external retention feature shall not be removed or adjusted unless this is essential to conduct the test, in which case, it shall be removed by carefully cutting the sheath as close as possible to the retention feature.

J.3.4 Precondition the female condoms, out of their individual containers, prior to testing under controlled conditions at a temperature of (25 ± 5) °C and relative humidity of (55 ± 15) % for a minimum of 18 h and a maximum of 72 h. Humidity control is not required for female condoms with a sheath made of natural rubber latex. Female condoms that are supplied pre-lubricated with a water-based lubricant shall be preconditioned in their individual containers at a temperature of (25 ± 5) °C.

J.3.5 Carry out the test at a controlled temperature of (25 ± 5) °C. When testing female condoms other than those made from natural rubber latex, the relative humidity shall also be controlled at (55 ± 15) %.

J.3.6 Hang the female condom on the test mount (rod or mandrel) and secure the base of the female condom with the clamping device.

J.3.7 Take care when placing the clamping device on its mount to avoid damaging or stretching the female condom. Inflate the female condom at a rate of (0,4 dm^3/s to 0,5 dm^3/s) (24 dm^3/min to 30 dm^3/min).

J.3.8 Check to ensure that the female condom expands and there are no obvious leaks.

J.3.9 If the female condom exhibits an obvious leak, the test should be discontinued because the condom might never burst. The female condom should be replaced and the test continued.

J.3.10 If the female condom does not leak, measure and record the bursting volume, in cubic decimetres rounded to the nearest 0,1 dm^3 if the minimum burst volume is 14,9 dm^3 or lower and to the nearest 0,5 dm^3 if the minimum burst volume is above 14,9 dm^3. The bursting pressure, in kilopascals, shall be rounded to the nearest 0,05 kPa. Record female condoms as non-conforming if they burst below the minimum bursting pressure and volume. If a female condom is observed to leak after reaching the minimum bursting pressure and/or volume, it should be counted as conforming.

J.4 Expression of results

Record the bursting volume and bursting pressure of each tested female condom.

Annex K
(normative)

Testing for holes

K.1 General

This annex specifies the water leak method for testing female condoms for visible and non-visible holes and visible defects.

K.2 Water leak test

K.2.1 Principle

Female condoms are visually inspected then filled with water and examined for visible water leakage through the wall of the suspended female condom. To prevent excessive stretching of female condoms made from highly extensible materials such as natural rubber latex, the maximum volume of water that can be added is limited to provide approximately the same degree of stretching experienced by natural rubber latex male condoms when being subjected to the equivalent test.

In the absence of any leakage, the female condom is then rolled on a coloured absorbent paper which is subsequently examined for signs of leakage of water from the female condom. Female condoms may be tested with or without the external retention device.

K.2.2 Apparatus

K.2.2.1 Water leak test plug or mount, suitable for filling the female condom with water while suspended and having a watertight fit with the open end of the female condom with or without the external retention device and a means of preventing water loss after filling such as a stopper. An informative example is shown in Figure K.1. The critical dimensions appropriate for each female condom design shall be made available. The plug may have a tapered shape that extends into the female condom to aid the technician in guiding the external retention feature onto the test plug. This feature shall allow as much as possible of the open end to be tested and inspected. A clamping ring might be required to retain the female condom on the mount or plug.

K.2.2.2 Water leak testing rack, suitable for allowing the female condom to be freely suspended by the test plug as shown in Figure K.2.

K.2.2.3 Absorbent towel.

K.2.2.4 Coloured absorbent paper.

K.2.2.5 Gloves.

K.2.2.6 Water.

K.2.2.7 Test rack.

K.2.2.8 Stopwatch.

K.2.3 Preparation

K.2.3.1 Wear suitable gloves when handling the female condoms so as to avoid damage to the female condom by fingernails, jewellery, etc.

K.2.3.2 To remove the female condom from its individual container, move the female condom inside the individual container so that it is away from the area where the individual container is to be torn. Tear the individual container and remove the female condom. Scissors or other sharp instruments shall not be used to open the individual container.

K.2.3.3 Unfurl or unfold the female condom and remove any non-permanently attached internal retention features and/or insertion devices. Do not remove or adjust the external retention feature.

K.2.3.4 Inspect the entire female condom for visible holes (see 3.1.14). If any hole or tear is noticed, the female condom shall be deemed non-conforming and further testing of that female condom shall be discontinued.

K.2.3.5 Inspect the entire female condoms for visible defects (see 3.1.15). If any visible defect other than a visible hole is noticed, the female condom shall be deemed non-conforming with respect to visible defects and further testing of that female condom shall be discontinued. If the defect is a visual hole, then the female condom shall be deemed non-conforming with respect to freedom from holes and further testing of that female condom shall be discontinued.

K.2.4 Procedure

K.2.4.1 Fit the female condom external retention feature around a water test plug or mandrel as shown in Figure K.2. Ensure the external retention feature is properly fitted on the test plug to ensure a leak-free seal. If visible abrasions or damage to the female condom are introduced during this fitting procedure, do not continue testing the female condom, move it to the drying rack and record that the female condom was not tested.

K.2.4.2 Calculate the maximum fill volume (MFV) for the condom using Formula K.1:

$$MFV = 1{,}9\, lw^2/1000\ \pi \qquad \text{(K.1)}$$

where

l is the nominal length of the female condom in mm;

w is the average of the nominal widths specified at 25 %, 50 % and 75 % along the length of the female condom from the closed end (see the determination of width in Annex E).

K.2.4.3 Add water at a temperature in the range of 10 °C to 35 °C to the female condom until either the condom is full or the calculated maximum fill volume is reached. With automated equipment, the fill volume may be determined and set in advance using a test condom. Intermittently tap the female condom to dislodge air bubbles and top off until the solution rises to the top of the test plug. Seal off the plug, for example, by inserting the stopper.

K.2.4.4 Dry the outside surface of the female condom with an absorbent towel. Inspect the female condom for leaks.

K.2.4.5 Suspend the female condom in the test rack as shown in Figure K.2 for a minimum of 1 min and a maximum of 3 min. Following suspension, visually inspect for any signs of leakage.

K.2.4.6 Remove the female condom and test plug or mount from the test rack. If no holes have been detected, roll the filled female condom on coloured absorbent paper while inspecting for leaks as shown in Figure K.3. Suspend the test plug over the edge of the testing table to maximize contact between the female condom and paper. Use even and firm hand pressure. Complete at least one whole rotation in each direction.

K.2.4.7 Examine the coloured absorbent paper for signs of leakage. If wet patches appear on coloured absorbent paper, locate the source of the leak. Continue the rolling until the leak has been found or it is determined that the initial wet patch was introduced by a means other than a female condom leak.

K.2.4.8 Twist the female condom just below the midway position to create two sections of the filled female condom as shown in Figure K.4. Press the female condom distal end into the coloured absorbent paper to ensure all female condom surfaces are tested as shown in Figure K.5. Examine the coloured absorbent paper for signs of leakage as described in K.2.4.7. Record all results and mark the location of any leaks found on the female condom.

K.2.4.9 Determine the location of any marked holes by placing the female condom on the length measurement mandrel described in Annex D, letting it hang freely stretched only by its own mass and measuring the distance between the marked hole and open end projected onto the scale.

K.3 Interpretation of test results

Female condoms with non-visible holes greater than 25 mm from the open end and female condoms with visible holes and visible defects are considered non-conforming.

K.4 Test report

Upon completion of the test, record the following data:

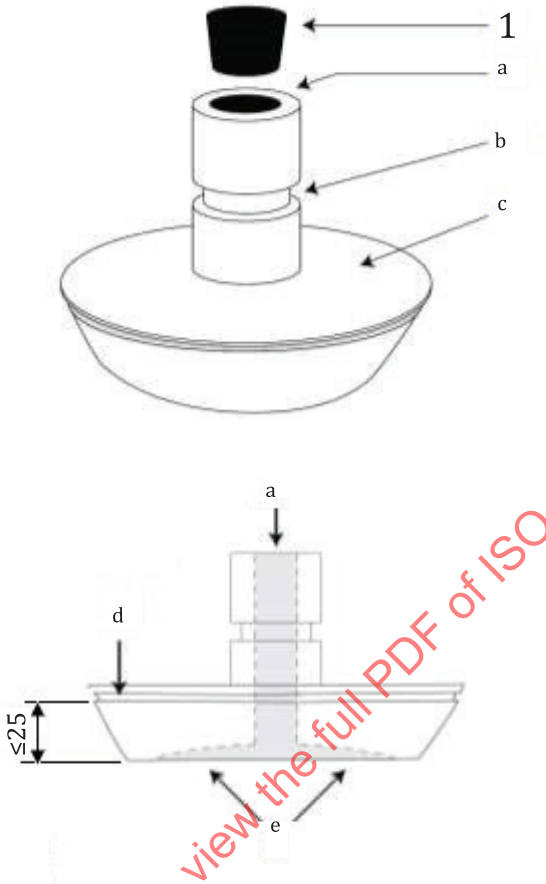
a) the number of female condoms tested;

b) the number of condoms with visible holes;

c) the number of condoms with non-visible holes located more than 25 mm from the open end;

d) the number of condoms with visible defects observed.

Dimensions in millimetres



Key

1 stopper
a Filling orifice.
b Testing rack groove.
c Water leak test plug.
d Groove geometry sized to fit specific device external retention feature.
e Dashed lines indicate preferred geometry to allow air bubbles to escape.

Figure K.1 — Example of a test plug with rubber stopper