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Male condoms — Guidance on the use of ISO 4074 and ISO 23409 in the quality management of condoms

Préservatifs masculins — Lignes directrices sur l'utilisation de la norme ISO 4074 et ISO 23409 sur le management de la qualité des préservatifs en latex de caoutchouc naturel et en matériau synthétiques

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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 second edition cancels and replaces the first edition (ISO 16038:2005), which has been technically revised, considering the revisions to ISO 4074 and the publication of ISO 23409. The modifications are as follows.

a) The title and Scope have been expanded to include ISO 23409 and the relevant aspects of synthetic male condoms have been added in this edition. The major points incorporated are with respect to design, determination of limits for burst properties, stability studies and clinical trials.

b) The revision to ISO 4074 and points arising out of the publication of ISO 4074:2015 have been incorporated in the guidance document.

c) An explanation regarding the application of switching rules in sampling in accordance with ISO 2859-1 has been incorporated.

d) The section on design has been expanded to explain significant changes to condoms, which warrant validation.

e) The principle of estimating shelf life of natural rubber latex condoms has been revised to reflect the principles of shelf determination as given in ISO 4074:2015.

f) The section on testing has been revised to include the modifications to test methods for determining freedom for holes.

g) The section on dimensions has been revised to include the aspects of tolerances for thinner condoms.

h) The aspects of condoms of smaller and larger sizes than those specified in ISO 4074 have been incorporated.

i) The impact of new test for visibly open seals as given in ISO 4074 and potential rework has been addressed.

j) The control of maximum storage period of naked condoms before packing them in individual sealed containers has been incorporated in accordance with ISO 4074.

Introduction

Condoms are medical devices used for contraception and for prevention of sexually transmitted infections.

ISO 4074 is a quality standard for natural rubber latex condoms and ISO 23409 for condoms made from synthetic materials. They are reference documents for standardized end product quality test protocols and a baseline specification for critical attributes that affect condom safety and effectiveness. They are applied by manufacturers, procurement agencies, regulatory bodies and testing laboratories.

The use of ISO 4074 and or ISO 23409 does not by itself ensure consistency in quality; consistent high quality at the lowest possible cost is attained only through a regime termed quality management, through which, quality is built into the product and ensured at every point in the design, planning, production and procurement processes. This document should lead to continuous improvement in manufacturing, procurement and testing processes. The special requirements of buyers and consumers should also be given due consideration when applying ISO 4074 or ISO 23409, as ISO 4074 and ISO 23409 are general by design, and will not cover all circumstances completely.

This document provides guidance to manufacturers, buyers and third-party test laboratories on implementing and applying ISO 4074 in the manufacture of condoms, and to purchasers on applying ISO 4074 or ISO 23409 and verifying that the condoms delivered conform to the specification, as appropriate.

Acceptable condoms meet or exceed the minimum requirements specified in ISO 4074 or ISO 23409, as applicable.

It is not possible, nor is it required, to subject condoms to user trials on a batch-by-batch basis. For this reason, certain evaluations are carried out only in the case of a pre-market validation; for example for new or significantly modified designs.

Design validation requirements normally include all the good manufacturing practice (GMP) validation requirements and the validation requirements of ISO 9001 and ISO 13485; these are not currently covered by ISO 4074 and ISO 23409, but are generally included by regulatory authorities as prerequisites for registering new designs of medical devices. Design considerations such as stability testing, etc., are, however, covered in ISO 4074 and evaluation of barrier properties by clinical trials and determination of burst properties are covered in ISO 23409.

ISO 4074 and ISO 23409 are mainly concerned with finished product testing carried out to monitor or to verify that the condoms have been manufactured with an adequate level of consistency in quality. For this purpose, tests have been designed that can be carried out rapidly and economically. The requirements in ISO 4074 and ISO 23409 are based on those properties which, based upon current knowledge, are believed to be relevant to the performance of condoms in normal use.

Some important properties of condoms are nevertheless difficult to define in quantitative terms because of a lack of controlled studies, the absence of practical and economical tests, and the need for different specifications to suit different users. ISO 4074 and ISO 23409 are, therefore, focused on the essential properties where limits can be clearly defined. Other properties are addressed only in general terms and are meant to be augmented through appropriate manufacturing records, certification by the manufacturer or by buyers' specifications.

This document also addresses how to deal with other related important issues not covered by ISO 4074 and ISO 23409.

It is meant to help the user of ISO 4074 and ISO 23409 to understand any risks that can be associated with the use of condoms. It also helps in deciding whether such risks are acceptable when weighed against the benefits to the condom user. ISO 4074 and ISO 23409 also help in assessing whether the products are demonstrably safe and offer protection to health. Good communication between the

buyer and the manufacturer will result in the delivery of satisfactory and safe products, thus avoiding unnecessary testing or inappropriate specifications, and thereby minimizing conformity testing costs.

NOTE In many countries, condoms, being medical devices, are subject to regulations.

The requirements for quality management are given in standards such as ISO 9001 and ISO 13485. ISO 9001 is based on the approach of achieving business excellence through quality management. For condoms, being a medical device, it is appropriate that ISO 13485 is applied for quality management as part of compliance to regulatory requirements.

Male condoms — Guidance on the use of ISO 4074 and ISO 23409 in the quality management of condoms

1 Scope

This document provides guidance on using ISO 4074 and ISO 23409 and addresses quality issues to be considered during the development, manufacture, quality verification and procurement of condoms. It encompasses the aspects of quality management systems in the design, manufacture and delivery of condoms with an emphasis on performance, safety and reliability.

Male condoms are either made from essentially natural rubber latex, in which case the requirements of ISO 4074 are applicable, or from synthetic materials and/or blends of synthetic materials and natural rubber latex, in which case the requirements of ISO 23409 are applicable. This document outlines the aspects applicable to both types of condoms with specific clarifications where appropriate.

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 4074:2015, *Natural rubber latex male condoms — Requirements and test methods*

ISO 9000, *Quality management systems — Fundamentals and vocabulary*

ISO 13485, *Medical devices — Quality management systems — Requirements for regulatory purposes*

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

ISO 23409:2011, *Male condoms — Requirements and test methods for condoms made from synthetic materials*

3 Terms and definitions

For the purposes of this document, the terms and definitions given in ISO 4074, ISO 9000, ISO 13485, ISO 14971 and ISO 23409 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 https://www.iso.org/obp

4 Quality of design

4.1 General

A condom is a single-use medical device, the performance and safety of which depends upon the design and the manufacturing process. New designs of condoms can require clinical testing, several other tests and analysis on a limited basis for validation purposes, such as shelf-life determination (type testing) and risk assessment. These requirements are generally prescribed by licensing authorities and the data generated become part of the master file for the product. Guidelines are available in ISO 13485

and the GMP requirements. When new products are developed, their design should conform to the requirements of design control as laid down in ISO 13485 and applicable GMP requirements.

The design control principles should be applied to parameters including

— condom shape;

— dimensions;

— critical components in formulation, such as base materials, antioxidants, vulcanizers, stabilizers, colourants, etc.,

— lubricants and additives such as flavour,

— additional lubricants etc., and

— packaging materials.

The safety of the materials used should be reviewed and ensured in accordance with applicable requirements.

NOTE For example, Medical Device Directive 93/42/EEC.

Design control activities should be documented as part of the quality management system documentation, reviewed and updated, when regulatory agency and/or customer needs warrant changes.

Whenever significant changes are made to the formulation or process that can substantially affect the performance and/or safety of the condoms, these changes should be evaluated, validated and documented.

EXAMPLE Changes in types of formulation, changes in lubricant, changes in primary (individual) packaging material, changes in leaching process.

Significant change is described as any change carried out to the approved design or process with the scope to materials, including packaging, formulation, manufacturing process, facilities or equipment, which can impact on performance, intended use, shelf life or other safety aspects, and which cannot be clearly excluded by a risk analysis.

Process validations should be carried out in accordance with the requirements of ISO 9001 or ISO 13485.

The design of synthetic condoms and the materials used result from consideration of the variety of materials possible and the need to meet the requirements of efficacy, adequate barrier properties and mechanical strength. The efficacy is evaluated through surrogate virus tests using bacteriophage Phi-X174, followed by clinical trials using comparison against natural rubber latex condoms as reference. Guidance on conducting *in vitro* viral penetration tests is given in documents such as the USFDA Guidelines and published literature. The penetration of bacteriophage Phi-X174 in test condom design should be evaluated with reference to approved design and levels published in literature. The median level of penetration has been reported to be $7 \times 10^{(-4)}$ ml. Details of conducting viral penetration tests, including limit of detection of the method and statistical interpretation of results, are given in ISO 23409:2011, Annex G.

Design validation should be used as the basis for ensuring that design parameters, such as dimensions, formulation, safety of components and biocompatibility, stability and shelf-life claims, packaging and dressing materials, etc., are appropriate. The biocompatibility studies should be done as per the requirements of ISO 10993-1, ISO 10993-5, ISO 10993-10 and the reports should be evaluated by a qualified toxicologist. When appropriate or necessary, such as when there has been a significant change in the formulation, skin irritation studies and a safety evaluation should be performed and documented as part of design control activities.

Purchasers, including procurement agencies, in addition to assuring that condoms conform to ISO 4074 or ISO 23409, should interact with manufacturers in specifying the parameters if the methods specified

in ISO 4074 and ISO 23409 are not applicable. Parameters include dimensions, type and amount of lubricant, tolerance in the amount of lubricant agreed between the manufacturer and procurement agencies, the method of determination of lubricant, type of packing, configuration of secondary and tertiary packaging, specific labelling. The shape, colour and additional features, if any, should also be stated by the procurement agency and agreed upon with the manufacturer. Any additional specifications should be communicated to the testing laboratories so that the correct specifications are applied when testing the products.

4.2 Clinical investigation

Since condoms are medical devices, it may be appropriate to carry out clinical trials rather than relying on laboratory data when significant changes are made to the design, type of lubricant, etc., and or when new materials are used and new claims are made. Clinical trials may also be conducted to compare specific characteristics of different products. These characteristics can include donning, slippage and breakage studies, and other parameters that can affect the efficacy and safety of condoms. Clinical trials should be conducted under a written protocol to monitor the objectives clearly stated in accordance with ISO 14155 and ISO 29943-1. Due consideration should be given to the inclusion of appropriate reference condoms. The risk management should be carried out as specified in ISO 14971. ISO 16037 is a guidance document that recommends physical parameters that should be measured before conducting clinical trials. The clinical data thus generated should be reviewed as required to ensure continued safety and conformity to the performance requirements of the condoms.

In the case of condoms made of synthetic materials, the values of physical properties measured form the basis for arriving at acceptance criteria for lot testing as part of quality verification as given in ISO 23409. Since the synthetic material can vary from design to design, the limits for arriving at acceptable minimum requirements of physical properties are derived based on the type testing results of the batches which are subjected to clinical investigation. The minimum requirements should be specified based on percentile values of individual condoms. Percentiles represent the value of parameters below which a certain percent of the observation falls.

4.3 Risk management

4.3.1 Risk analysis and risk management

Manufacturers should carry out risk management as specified in ISO 14971 and make the risk management report available to institutional purchasers and regulatory agencies upon request within a framework of confidentiality. Any claims of additional features should have definite substantiated performance and safety data should be duly documented (e.g. for extra-strength condoms).

As an important component of risk management, the manufacturer should inform the user, through labelling, of any properties of the product or substances contained within it that can cause irritation, sensitization or allergic reaction. Guidelines for labelling are specified in ISO 4074 and ISO 23409, as applicable. Attention should be given to the appropriate choice of colours and additives, which are approved by regulatory agencies or certified to be safe for use in human beings. The user should be advised of the potential for allergy in rare cases due to latex or other chemicals present in the formulation.

4.3.2 Latex allergy

Condoms made from natural rubber latex or its blend release smaller amounts of protein than latex gloves as they have thinner films and shorter duration of usage. However, latex condom manufacturers should strive to keep the latex-protein level minimal. Control of extractable proteins is a quality management issue, and the manufacturer should be aware of and control the content and release of allergenic substances, such as extractable proteins, by appropriate process steps and controls; the process steps and controls should be part of the manufacturer's quality management system. The methods for determining protein levels in latex products are given in ASTM D5712-99.

These methods can be adapted to determine protein levels in condoms. Protein levels can also be determined by the ELISA method given in ASTM D6499-03.

No limits for protein levels are established in ISO 4074 and ISO 23409.

4.3.3 Microbial contamination (bioburden)

Although condoms are non-sterile medical devices, care should be taken during manufacturing operations to minimize microbiological contamination, particularly specific pathogens that affect the skin and mucosa. For example, various species of pseudomonas, staphylococcus and *E. coli*. The potential causes of contamination should be identified, controlled and monitored through the quality management system.

ISO 4074 requires that manufacturers should establish procedures for periodic monitoring of microbial contamination (bioburden) as part of their quality management system. The procedure should be based on the risk analysis done by the manufacturer with respect to microbial contamination such that the method for determining bioburden levels, periodicity of monitoring and limits for total viable counts are established to ensure safety of the condoms manufactured. It is suggested that the determination of bioburden is done on condoms at different stages of manufacture and different environmental conditions prevailing in critical manufacturing and storage areas, and appropriate limits and frequency of monitoring are established. Regular trend analysis of data will be helpful in effective monitoring and taking required preventive and corrective actions for avoiding contamination. ISO 4074 requires that specific pathogens be absent. The methods for determining bioburden levels are given in ISO 4074:2015, Annex G.

4.3.4 Nitrosamines

Condoms made from natural rubber latex are subject to considerations regarding nitrosamines. Although the level of nitrosamines depends upon the formulation used by different manufacturers, the level of nitrosamines released by condoms is considered generally safe. Manufacturers are conscious of this development and are advised to monitor the levels of nitrosamines in their condoms. A method for the determination of nitrosamines migrating from natural rubber latex condoms into water is given in ISO 29941.

5 Quality of manufacture

5.1 Quality management

The principle behind quality management is that quality cannot be achieved effectively and consistently through end product testing alone. Rather, it should be built into every stage of the process and related activities that have direct impact on the quality of the product. The manufacturer should apply the requirements of ISO 9001, ISO 13485 or other similar standards as the basis for quality management system and for its good manufacturing practices for medical devices. These documents help to put into operation the principles of quality management in the design and manufacture of products, and are generally required and emphasized for production of health-related products throughout the world. They ensure that products are manufactured with clear and appropriate quality objectives and require that the quality management systems of manufacturers are subject to regular audits to ensure the effectiveness and continual improvement of the systems. Procurement agencies and regulatory bodies should encourage and support manufacturers who implement a quality management system as described above.

5.2 Lot testing (finished product testing)

Manufacturers should establish appropriate procedures to ensure that each lot conforms to the requirements of ISO 4074 or ISO 23409, as applicable and any additional requirements agreed with the purchaser. Manufacturers may test every lot or establish appropriate statistical control procedures to ensure conformity. Because testing is destructive, tests are conducted on samples drawn in accordance

with ISO 2859-1 or equivalent. Sampling plans and conformity levels are given in ISO 4074 and ISO 23409 and these should be incorporated into the manufacturers' quality systems. When applying the sampling plan, it should be emphasized that the switching rules specified in ISO 2859-1 should be implemented to offer necessary customer protection. The switching rules specified in ISO 2859-1 prescribe the necessary sampling plans, the review of sample testing results from continuing series of lots, and the switch to tightened or reduced sampling plans, as per the switching score. These requirements have been prescribed in order to correctly apply the statistical principles involved in the operating characteristics curves. They consider the impact of failure or acceptance of one or more lots to the quality of other lots involved in a continuing series of lots. While they offer the advantage of reduced sample sizes when the quality of is consistent in a series of lots, they also demand tighter accept/ reject levels when the quality is marginal or poor due to multiple failure in a series of lots. Manufacturers are advised to improve their production facilities to the stage where they can establish more stringent internal conformity levels than those in ISO 4074 and ISO 23409, to maximize acceptance by purchasers and third-party testing laboratories. Trends in lot quality can be used by manufacturers to monitor their quality, and to give early warning that corrective action is needed to keep the product quality within acceptable limits. Regulatory authorities and large purchasers can also examine trends and long-term performance of manufacturers to get a better assessment of the quality of products supplied by particular manufacturers. Manufacturers are advised to establish more stringent internal conformity levels to maximize yields. Trends in lot quality can be used by manufacturers or purchasers to further assess the quality management of the individual manufacturer. Regulatory agencies and purchasers may employ certified or accredited third-party laboratories for testing lots of products in addition to periodic audits of a manufacturer's quality management system.

In cases of dispute where manufacturers and purchasers have agreed to retest a lot, it is recommended to use the appropriate sampling plans given in ISO 4074:2015, Annex B, or ISO 23409:2011, Annex B.

Alternate plans, if required and when applicable should be agreed between the manufacturer and the purchaser.

5.3 Rounding-off values

The results obtained during testing of samples are rounded as given in the relevant clauses of ISO 4074 and ISO 23409. Where not specified in ISO 4074 and ISO 23409, the rounding rules specified in ISO 80000-1:2009, Annex B, should be followed.

6 Quality in procurement

When procuring condoms, institutional purchasers should define the specifications for condoms considering the population to which the condoms are sold or distributed. Procurement agencies should validate the source from which the condoms are procured by using pre-qualification assessment and periodic audit of the facilities and quality management system by an auditor familiar with condom manufacturing and type testing of samples.

Traceability of the materials and process used in the manufacture of condoms is important and should be implemented and monitored as required by ISO 13485, as part of a manufacturer's quality management systems.

If condoms are to be purchased from a distributor rather than a manufacturer, it should be ensured that there is traceability of the product to the manufacturer and that there is traceability within the manufacturer's production systems. When selecting the sources, the quality and reliability of manufacturers should be reviewed with additional weight given to manufacturers who exceed the basic requirements of ISO 4074 or ISO 23409, as applicable, by addressing additional measures such as the implementation of quality management systems, and special issues such as the stability of products, safety of products, control of bioburden, etc. The reliability of manufacturers should be further assessed on the basis of continuous supplies confirmed by end product testing and adherence to delivery schedule, price and the technical support services they provide. The objective of ensuring an undisrupted timely supply of quality condoms can only be achieved by selecting the right sources followed by continuous monitoring of supplies from those sources in addition to end product testing.

The results of lot-by-lot testing should be monitored for each manufacturer. Any dispute in lot-by-lot testing should be reviewed considering all the relevant aspects and making use of advice as outlined in Reference [34].

Appropriate design and packaging specifications should be obtained when procuring condoms, considering the needs of the population and the logistics of procurement, promotion, storage, handling and distribution. Due attention should be given to the storage of condoms in cool places that are adequately protected from harmful weather conditions, direct heat, sunlight and mechanical damage. Condoms should be procured with shelf-life claims duly supported by stability data. Distribution should be managed in such a way that the stocks are utilized well before their expiry date, using effective inventory management. Batch identification and traceability are important aspects of quality management systems, which are relevant during the handling, storage and distribution of condoms.

When procuring condoms, marginal issues on specifications and disputes on testing should be handled on the basis of technical expertise and guidelines, rather than by mere administrative provisions. The purchaser should seek advice from technical experts on condoms and make a balanced decision weighing the risks and availability of safe and reliable condoms.

NOTE The WHO offers a helpline service[34].

7 Quality in testing

Third-party laboratories are widely used for the procurement of condoms and regulatory monitoring. They should be selected on the basis they have a certified quality management system (e.g. ISO 9001) or are accredited in accordance with ISO/IEC 17025 by a recognized body. Since conformity testing of condoms based on ISO 4074 or ISO 23409 requires reliable detection of low levels of defectives tested by attributes (e.g. 0,25 AQL) based on sampling plans specified in ISO 2859-1, the performance of laboratories should be suitably monitored by interlaboratory testing and calibration programmes. The third-party test laboratories should have adequate expertise in implementing the intricacies of sampling plans as elaborated in ISO 2859-1. The monitoring of third-party laboratories by procurement agencies should be based on periodic audits and review of interlaboratory test programmes. Accredited laboratories should be periodically audited by national accreditation agencies.

8 Important parameters to consider when using ISO 4074 and ISO 23409

8.1 Application of ISO 4074 and ISO 23409

It is important to note that for male condoms made from natural rubber latex, because of considerable experience accumulated over the years, the specifications and limits have been arrived at based on the fitness for purpose and the level of the current state of technology. For male condoms made from synthetic materials, because of the variety of materials involved and the limited level of experience, the specifications are design specific and are not intended to be design restrictive. In arriving at such specifications, the efficacy and safety are evaluated for each design and type by comparison with pre-existing, clinically proven designs or types. The requirements of specifications for each of the parameters are based on the data on lots submitted for regulatory approval, relating to lots used for clinical trials to prove efficacy, safety and stability.

8.2 Dimensions

There is evidence that in different parts of the world, different condom sizes are needed. There appears to be a need for providing a range of sizes. A condom that is too small can cause problems in unrolling; one that is too large can slip off during use. The range of comfortable fit for any given size will also depend upon the properties and shape of the particular condom design. Any increase in the number of sizes would complicate production and increase costs. Some new sizes can have a market too small to be economical. For natural rubber latex condoms, condoms that have a mid-body width less than 45 mm and/or are shorter than 160 mm excluding the reservoir tip cannot be claimed to meet the requirements of ISO 4074.

Regulatory authorities and buyers should be aware of the appropriate size(s) for their user populations.

If they believe that different sizes are needed, appropriate studies would help to establish confidence in the need for additional sizes. ISO 4074:2015, Annex P, includes recommendations on appropriate modifications to test methods for determining critical parameters, such as freedom from holes and burst properties for condoms falling outside the specified range. Marketing of these products is at the discretion of the appropriate regulatory authorities or notified bodies.

Measurement of the thickness of condoms has always been a matter subject to inconsistencies in reproducibility and specification of limits. ISO 4074 specifies methods for measurement and the limits of tolerances depending upon the various ranges of condoms, including those condoms which claim lower thicknesses.

ISO 4074:2015 prescribes appropriate tolerance ranges for measurement of the thickness of thinner condoms.

8.3 Visibly open seals

ISO 4074 introduces a test for visibly open seals for individual sealed containers for natural rubber latex condoms. This requirement has been introduced because partial or fully open seals can compromise the stability of condoms and allow leakage of lubricant. The requirement includes the acceptance quality limit (AQL) for the parameter. It is possible that in some instances the manufacturer can rework a lot that fails this test. Any rework should conform to the requirements of rework and sampling as specified in ISO 2859-1. There should be a detailed risk assessment for any such rework process.

8.4 Justification of additional claims

Condoms should have sufficient elasticity and mechanical strength. The determination of burst volume and pressure by inflation of air provides a reasonable measure of the quality and consistency of the condom. Tests for tensile properties also measure stress and strain. However, claims such as “extra strong” should not be assumed to offer higher level of protection against breakage, unless substantiated by clinical data. Any claim that directly or indirectly implies increased safety and performance should be substantiated by a well-designed and executed clinical evaluation. The breakage of condoms can also be caused by improper use and inadequate lubricity in use. The clinical data should substantiate a statistically significant reduction in breakage rate for the extra strong condom when compared to a reference, marketed condom from normal production produced by the same manufacturer. The reference condom should conform to the requirements of ISO 4074 and should exceed 0,060 mm single wall thickness at mid-body.

In the case of synthetic condoms, the limits for burst volume and burst pressure are design specific, based on the lots used for type testing at the time of regulatory approval in relation to the lots used for clinical trials.

8.5 Compatibility of materials

Oil-based lubricants are often easily available to users but should not be used with condoms. They degrade the latex film so quickly that the condom can fail during the period of normal use. This issue is dealt with in ISO 4074 in the relevant clause on labelling. The compatibility of topical drugs used in the vagina with condoms cannot be assumed and drug manufacturers should be encouraged to do compatibility tests. Additional lubricants, when used, should be carefully chosen (see 8.8). Materials used in the manufacture of condoms, including foiling and packaging, should be proven to be compatible with the product by appropriate assessments during the design and manufacturing stages.

For synthetic condoms, an evaluation should be made of the chemical compatibility of the materials used, as well as with other materials and body fluids that can come into contact with such condoms.

8.6 Freedom from holes

For natural rubber latex condoms, any of the methods given in ISO 4074:2015, M.2 or M.3, for the water leak test or the electric test, respectively, should be followed. The sensitivity electric test method has been substantially revised in ISO 4074:2015 to improve the sensitivity of the method. Work is in progress to improve the sensitivity further.

The method for testing for freedom from holes specified in ASTM D3492 can also be used.

However, due to limited information on the applicability of the electric test to a variety of synthetic materials, some of which can be electrically conductive to varying levels, the electric test should be validated, as prescribed in ISO 23409:2011, Annex J.

8.7 Shelf life and resistance to degradation

ISO 4074:2015, Clause 11, addresses the requirements of stability and shelf life of condoms. This clause covers minimum stability requirements (11.2), real time stability studies (11.3) and accelerated stability studies (11.4).

It should be established, by design control, that condoms will have adequate resistance to degradation during the claimed shelf life. Incorporation of suitable antioxidants and preservatives in the formulation, using metal-based foil laminates with excellent barrier properties and labelling instructions detailing proper storage conditions will ensure protection during storage. These aspects should be validated at the design stage, monitored during manufacture and confirmed by type testing, when required.

Shelf-life considerations are important for ensuring that the physical, performance and safety aspects of condoms are met throughout the claimed period. Only condoms properly formulated and suitably processed and packaged will be able to meet the specifications during shelf life. The quantity and nature of antioxidant, vulcanizing chemicals and stabilizers are all critical in conferring the requisite shelf life. Condoms tend to undergo degradation by oxidation and decomposition of materials of condom structure. They should be stored in a way that protects them from light, heat and mechanical damage so the properties are not affected. Therefore, it is recommended to protect condoms by packing them in oxygen- and ozone-impermeable materials, such as aluminium-foil laminates, and to protect them from light-catalysed degradation reactions.

The shelf-life claims should refer to the date of manufacture and claimed expiry date.

The requirements regarding shelf-life claims, assigning date of manufacture and claimed expiry date in relation to storage of bulk products before packing within individual containers are given in ISO 4074:2015, 11.1.

In the case of natural rubber latex condoms, shelf-life claims should be substantiated by well-designed stability studies, in accordance with ISO 4074:2015, Clause 11. Shelf life should be determined by real time studies at (30^{+5}_{-2}) °C.

ISO 4074:2015, 11.2 defines the minimum stability requirement for conformity before any new product for which there has been a significant change to formulation or process can be marketed. Even though this requirement does not correlate with any specified shelf life, it has been included in the standard essentially as a safeguard.

Corresponding requirements for condoms made from synthetic materials are prescribed in ISO 23409:2011, Clause 13.

Since it is impracticable to complete real-time ageing studies as given in ISO 4074:2015, 11.3 before introducing products to the market, accelerated stability studies based on kinetic principles can be used to assign a provisional shelf life. Such assigned, provisional shelf lives should be verified by real-time studies.

Manufacturers should carry out accelerated stability studies to predict shelf life. Such predicted shelf-life claims should be supported by real-time data. Methods for accelerated stability studies are

based upon models that can predict the outcome of real-time ageing studies. Accelerated stability studies can be conducted by the methods described and referred to in ISO 4074:2015, Annex L or ISO 23409:2011, Annex L, where applicable, or by other methods acceptable to the relevant regulatory authorities. Manufacturers who have historical real-time data on many different products are able to perform comparative tests between old and new products. Comparing accelerated test results of the new products with known ageing data, accelerated as well as real time, allows these manufacturers to determine the estimated shelf life for the new products.

The selection of temperatures and time periods for accelerated stability studies should be made with caution as there is only limited experience with the application of this technique.

Manufacturers who do not have an extensive historical database and third-party testers cannot rely on these methods and therefore may use methods based on kinetic models.

ISO 4074 also gives recommendations on assigning provisional shelf life based on accelerated stability studies conducted at (50 ± 2) °C.

ISO 4074:2015, L.2 describes a method for predicting shelf life for natural rubber latex condoms.

If all the lots are in conformity when tested as per the requirements given in ISO 4074:2015, Annex L, then the appropriate provisional shelf life can be assigned to the product depending on the conditioning period:

— a shelf life of 2 years after a period of 90 days;

— a shelf life of 3 years after a period of 120 days;

— a shelf life of 5 years after a period of 180 days.

ISO 4074:2015, L.3, describes a method for estimating shelf life based on accelerated stability studies by comparison with a control condom of established shelf life.

For convenience, the ageing temperatures can be selected as 70 °C and 50 °C and, provided the ageing periods at these temperatures equal or exceed 7 days at 70 °C and 90 days at 50 °C, then this test can also be used to verify the requirements of ISO 4074:2015, L.3.

The principles described in ISO 11346 can also be applied in conducting the accelerated shelf life studies and interpreting the results to estimate the proposed shelf life.

For synthetic condoms, appropriate temperature and relative humidity conditions should be used depending upon the nature of the material and the length of shelf-life claims made.

Given the limited experience of estimating shelf life by applying these techniques, ISO 4074 currently specifies that shelf life claims should not exceed five years.

8.8 Packaging and labelling

The packaging materials chosen should give the condoms appropriate protection from damage due to oxidation, UV-light, moisture, environmental contamination and mechanical damage during shipping, storage and handling. Labelling requirements are specified in ISO 4074:2015, Clause 15, or ISO 23409:2011, Clause 16, and can be supplemented with special requirements of the purchaser and the regulatory agencies of each country.

The shelf-life claims are related to specific storage conditions and hence the storage conditions, which form a part of labelling.

ISO 4074 has also introduced a quality verification requirement for the parameter of visibly open individual seals (see 8.3).

Markings on labels should be in accordance with applicable standards, such as ISO 15223-1 and ISO 15223-2 or EN 980.