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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

ISO (the International Organization for Standardization) is a worldwide federation of national standards bodies (ISO member bodies). The work of preparing International Standards is normally carried out through ISO technical committees. Each member body interested in a subject for which a technical committee has been established has the right to be represented on that committee. International organizations, governmental and non-governmental, in liaison with ISO, also take part in the work. ISO collaborates closely with the International Electrotechnical Commission (IEC) on all matters of electrotechnical standardization.

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).

Any trade name used in this document is information given for the convenience of users and does not constitute an endorsement.

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.