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Male condoms — Guidance on the use of ISO 4074 and ISO 23409 in the quality management of natural rubber latex condoms and synthetic condoms

Préservatifs masculins — Directives sur l'utilisation de l'ISO 4074 et de l'ISO 23409 dans le management de la qualité des préservatifs en matières synthétiques et en latex de caoutchouc naturel

[Revision of first edition (ISO 16038:2005)]

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Pour accélérer la distribution, le présent document est distribué tel qu'il est parvenu du secrétariat du comité. Le travail de rédaction et de composition de texte sera effectué au Secrétariat central de l'ISO au stade de publication.

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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.

International Standards are drafted in accordance with the rules given in the ISO/IEC Directives, Part 2.

The main task of technical committees is to prepare International Standards. Draft International Standards adopted by the technical committees are circulated to the member bodies for voting. Publication as an International Standard requires approval by at least 75 % of the member bodies casting a vote.

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.

ISO 16038 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) of which has been technically revised.

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 condoms. 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 assured at every point in the design, planning, production and procurement processes. This International Standard 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 completely all circumstances.

This International Standard is a guidance document providing manufacturers, buyers, and third-party test laboratories guidance to implement and apply ISO 4074 in the manufacture of condoms and for purchasers to apply ISO 4074 or ISO 23409 as a technical specification and to verify that condoms delivered, comply with the specification, as appropriate.

In order to be acceptable, condoms need to 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 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 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 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 International Standard also addresses how to deal with other 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 may be associated with the use of condoms. It also helps in deciding whether such risks are acceptable when weighed against the benefits to the 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, thereby minimizing compliance testing costs.

It should also be noted that in many countries condoms being medical devices are subject to appropriate 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 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 natural rubber latex condoms and synthetic condoms

1 Scope

This International Standard 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 design, manufacture and delivery of condoms with emphasis on performance, safety and reliability of condoms. Male condoms are either made from essentially natural rubber latex, in which case the requirements of ISO 4074 are applicable; or when male condoms are made from synthetic materials and or blends of synthetic materials and natural rubber latex, the requirements of ISO 23409 are applicable. This International Standard outlines the aspects applicable to both types of condoms with specific clarifications where appropriate.

2 Normative references

The following referenced documents are indispensable for the application 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 31-0:1992, *Quantities and units – Part 0: General principles*

ISO 2859-1, *Sampling procedures for inspection by attributes – Part 1: Sampling schemes indexed by acceptance quality limit (AQL) for lot-by-lot inspection*

ISO 4074, *Natural latex rubber 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 14155, *Clinical investigation of medical devices for human subjects*

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

ISO/IEC 17025, *General requirements for the competence of testing and calibration laboratories*

ISO 23409: –[1)] *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 and ISO 23409 apply.

1) To be published.

4 Quality of design

4.1 General

The 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 may 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 GMP requirements.

The design control principles should be applied to parameters such as shape of condoms; dimensions; critical components in formulation such as base materials, antioxidants, vulcanizers, stabilizers, colorants, 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 appropriate regulatory requirements such as Medical Device Directive. 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 may substantially affect the performance and/or safety of the condoms, these changes should be evaluated, validated and documented (e.g. changes in types of formulation, changes in lubricant, changes in primary (individual) packaging material, changes in leaching process).

Design of synthetic condoms and their materials are arrived at considering the variety of materials possible and the need to meet the requirements of efficacy, adequate barrier properties and mechanical strength. The efficacy is evaluates by using surrogate virus tests using bacteriophage Phi-X174, followed by clinical trials by comparison against natural rubber latex condoms as reference.

Design validation should be used as the basis for ensuring that design parameters such as dimensions, formulation, components, stability and shelf-life claims, packaging and dressing materials, etc., are appropriate. When appropriate or necessary, such as when there has been a significant change in the formulation, skin irritation studies and safety evaluation should be performed and documented as part of design control activities.

Purchasers including procurement agencies, in addition to assuring that condoms comply with the ISO 4074 or ISO 23409, should interact with manufacturers in specifying the parameters such as dimensions, type and amount of lubricant, type of packing, configuration of secondary and tertiary packaging, specific labelling, etc. 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 also so that the correct specifications are applied while testing the products.

4.2 Clinical investigation

Since condoms are medical devices, it may be appropriate to carry out clinical trials when significant changes are made to the design, type of lubricant, etc. rather than relying on laboratory data. Clinical trials may also be conducted to compare specific characteristics of different products. These characteristics might include donning, slippage and breakage studies, and other parameters that could affect the efficacy and safety of the condoms. Clinical trials should be conducted under a written protocol, to monitor the objectives clearly stated in accordance with ISO 14155 and ISO 29943. 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 compliance with performance requirements of the condoms.

4.3 Risk management

4.3.1 Risk analysis and risk management

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

As an important component of risk management, the manufacturer needs to inform the user, through labelling, of any properties of the product or substances contained in it that may cause irritation, sensitization or allergic reaction. Guidelines for labelling have been set by several regional and national regulatory authorities and also specified in ISO 4074 and ISO 23409, as applicable. Attention should be given to right choice of colours and additives, which are approved by regulatory agencies or certified to be safe for use in human beings. The consumer should be advised of potential of 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 have 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 needs to know about 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 gloves are given in EN 455-3 and ASTM D5712-99.

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

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

4.3.3 Bioburden

Although condoms are non-sterile medical devices, care should be taken during manufacturing operations, to minimize microbiological contamination, particularly specific pathogens which affect the skin and mucosa, for example various species of pseudomonas, streptococcus, staphylococcus and *E. coli*. The potential causes of contamination should be identified, controlled and monitored through the quality management system. No limits for bioburden are specified in ISO 4074 and ISO 23409. Reference is available in other standard such as ISO DIN 4074. Biological evaluation can also be carried out using the test method specified in ISO 10993-1.

4.3.4 Nitrosamines

Condoms made from natural rubber latex are subject to considerations regarding nitrosamines. Though the level of nitrosamines depend upon the formulation used by different manufacturers, the level of nitrosamines released by condoms are considered generally safe. No regulatory specification has been arrived as yet for this parameter. Manufacturers are conscious of this development and are advised to monitor the levels of nitrosamines in their condoms. A method for determination of nitrosamines migrating from natural rubber latex condoms into various media 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 needs to 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