ประกาศกระทรวงอุตสาหกรรม

ฉบับที่ ๓๘๑๘ (พ.ศ. ๒๕๕๑)

ออกตามความในพระราชบัญญัติมาตรฐานผลิตภัณฑ์อุตสาหกรรม

พ.ศ. ๒๕๑๑

เรื่อง กำหนดมาตรฐานผลิตภัณฑ์อุตสาหกรรม

ถุงยางอนามัย - แนวทางการใช้ ISO 4074

ในการจัดการคุณภาพถุงยางอนามัยจากน้ำยางธรรมชาติ

อาศัยอำนาจตามความในมาตรา ๑๕ แห่งพระราชบัญญัติมาตรฐานผลิตภัณฑ์อุตสาหกรรม พ.ศ. ๒๕๑๑ รัฐมนตรีว่าการกระทรวงอุตสาหกรรมออกประกาศกำหนดมาตรฐานผลิตภัณฑ์อุตสาหกรรมถุงยางอนามัย - แนวทางการใช้ ISO 4074 ในการจัดการคุณภาพถุงยางอนามัยจากน้ำยางธรรมชาติ มาตรฐานเลขที่ มอก. 2352 - 2550 ดังมีรายการละเอียดต่อท้ายประกาศนี้

ประกาศ ณ วันที่ ๒๑ มกราคม พ.ศ. ๒๕๕๑

โฆสิต ปั้นเปี่ยมรัษฎ์

รัฐมนตรีว่าการกระทรวงอุตสาหกรรม

มาตรฐานผลิตภัณฑ์อุตสาหกรรม
ถุงยางอนามัย - แนวทางการใช้ ISO 4074 ในการจัดการคุณภาพถุงยางอนามัย จากน้ำยางธรรมชาติ

บทนำ

มาตรฐานผลิตภัณฑ์อุตสาหกรรมนี้กำหนดขึ้นโดยรับ ISO 16038 : 2005 Rubber condoms – Guidance on the use of ISO 4074 in the quality management of natural rubber latex condoms มาใช้ในระดับเหมือนกันทุกประการ (identical) โดยใช้ ISO ฉบับภาษาอังกฤษเป็นหลัก

ขอบข่าย

มาตรฐานผลิตภัณฑ์อุตสาหกรรมนี้กำหนดแนวทางการใช้ ISO 4074 และครอบคลุมประเด็นต่าง ๆ ที่ต้องพิจารณาในการพัฒนาการผลิต การทวนสอบคุณภาพ และการจัดหาถุงยางอนามัย มาตรฐานผลิตภัณฑ์อุตสาหกรรมนี้ยังระบุถึงระบบการจัดการคุณภาพในเรื่องการออกแบบ การผลิต และการขนส่ง โดยเน้นในเรื่องสมรรถนะ ความปลอดภัย และความเชื่อถือได้ของถุงยางอนามัย

เอกสารอ้างอิง

รายละเอียดให้เป็นไปตาม ISO 16038 : 2005 ข้อ 2

บทนิยาม

ความหมายของคำที่ใช้ในมาตรฐานผลิตภัณฑ์อุตสาหกรรมนี้ให้เป็นไปตาม ISO 16038 : 2005 ข้อ 3

คุณภาพของการออกแบบ

รายละเอียดให้เป็นไปตาม ISO 16038 : 2005 ข้อ 4

คุณภาพของโรงงาน

รายละเอียดให้เป็นไปตาม ISO 16038 : 2005 ข้อ 5

คุณภาพในการจัดหา

รายละเอียดให้เป็นไปตาม ISO 16038 : 2005 ข้อ 6

คุณภาพในการทดสอบ

รายละเอียดให้เป็นไปตาม ISO 16038 : 2005 ข้อ 7

ปัจจัยสำคัญที่ต้องคำนึงถึงในการใช้ ISO 4074

รายละเอียดให้เป็นไปตาม ISO 16038 : 2005 ข้อ 8

การชักตัวอย่าง

รายละเอียดให้เป็นไปตาม ISO 16038 : 2005 ข้อ 9

Contents

Page

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. It is a reference document for standardised end-product quality test protocols and a baseline specification for critical attributes that affect condom safety and effectiveness. It is applied by manufacturers, procurement agencies, regulatory bodies and testing laboratories.

The use of ISO 4074 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, as ISO 4074 is 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 as a technical specification and to verify that condoms delivered, comply with the specification.

In order to be acceptable, condoms need to meet or exceed the minimum requirements specified in ISO 4074.

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; these are not currently covered by ISO 4074, 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.

ISO 4074 is 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 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 is 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. It is meant to help the user of ISO 4074 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 also helps 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.

Information about standards can be obtained through catalogues issued by ISO, IEC, national standards bodies and regulatory agencies. List of projects under development by various ISO technical committees can be found in the ISO technical programme of each committee. Additional useful information can also be found by searching in the work program documents for a specific technical committee or its working groups. The catalogues and abstracts are issued yearly to the member bodies.

Modern technology opens up the opportunity for new ways to disseminate information about standards. Many national member bodies issue information on CD-ROM. Information also can be found on the World Wide Web by searching for quality-related subjects or under ISO. It is possible to search for information by committees, by published standards, and in a standards catalogue. It is also possible to obtain information on the revision status of a standard and the expected time of publication. This information is updated regularly, and it is therefore an extremely useful tool to search for standards in a given field and the stage of development.

— ISO on-line has the address http://www.iso.org;

— IEC on-line has the address http://www.iec.ch.

On both of these servers, links to member bodies which also have additional services are available, sometimes by subscription.

Other useful documents are given in the Bibliography.

Rubber condoms — Guidance on the use of ISO 4074 in the quality management of natural rubber latex condoms

1 Scope

This International Standard provides guidance on using ISO 4074 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.

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 4074:2002, *Natural latex rubber condoms — Requirements and test methods*

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

ISO 14155-1, *Clinical investigation of medical devices for human subjects — Part 1: General requirements*

ISO 14155-2, *Clinical investigation of medical devices for human subjects — Part 2: Clinical investigation plans*

3 Terms and definitions

For the purposes of this document, the terms and definitions given in ISO 4074 and ISO 9000 apply.

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 9000 and the GMP requirements. When new products are developed, their design should conform to the requirements of design control as laid down in ISO 9001 and GMP requirements.

The design control principles should be applied to parameters such as shape of condoms; dimensions; critical components in formulation such as antioxidants, vulcanizers, stabilizers, colorants, etc.; lubricants and additives such as flavour, additional lubricants etc; and packaging materials. 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 lubricant, changes in primary (individual) packaging material, changes in leaching process).

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, 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 14155-1 and ISO 14155-2. Due consideration should be given to the inclusion of appropriate reference condoms. The risk analysis 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.

4.3 Risk management

4.3.1 Risk analysis and risk management

The manufacturers should carry out risk analysis as specified in ISO 14971 and make the analysis 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. 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 latex allergy in rare cases.

4.3.2 Latex allergy

Condoms 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.

2

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. Biological evaluation can also be carried out using the test method specified in ISO 10993-1.

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 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 complies with requirements of ISO 4074 and any additional requirements agreed with the purchaser. Manufacturers may test every lot or establish appropriate statistical control procedures to ensure compliance. Because testing is destructive, tests shall be conducted on samples drawn according to ISO 2859-1 or equivalent. Sampling plans and compliance levels are given in ISO 4074 and these need to be incorporated into the manufacturers' quality systems. While applying the sampling plan, it should be emphasized that switching rules as specified in ISO 2859-1 should be implemented to offer necessary customer protection. Manufacturers are advised to improve their production facilities to the stage where they can establish more stringent internal compliance levels than those in ISO 4074, 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 suppliers to get a better assessment of the quality of product supplied by particular manufacturers. Manufacturers are advised to establish more stringent internal compliance 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 manufacturer's quality management system.

In cases of dispute where manufacturers and purchasers have agreed to retest a lot, it is recommended the appropriate sampling plans given in Annex B of ISO 4074:2002 or an alternate plan be used.

5.3 Rounding-off values

The results obtained during testing of samples are to be rounded off as given in relevant sections of ISO 4074. Where not specified in ISO 4074, follow the rounding-off rules specified in ISO 31-0:1992, Annex B.

6 Quality in procurement

While procuring condoms, the institutional purchasers should define the specifications for condoms considering the population to which the condoms are sold or distributed. It is necessary for the procurement agencies to

validate the source from which condoms are procured by pre-qualification assessment, by 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 the process used in manufacture of condoms is important and should be implemented and monitored as required by ISO 13485, as part of 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 product to the manufacturer and that there is traceability within the manufacturer's production systems. While 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 by addressing additional measures such as implementation of quality managements, and special issues such as stability of products, safety of products, control of bioburden, etc. The reliability of manufacturers should also be assessed further on the basis of continuous supplies confirmed by end product testing and adherence to delivery schedule, price and technical support services rendered by the manufacturers. The objective of ensuring undisrupted timely supply of quality condoms can be achieved only 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 a document by WHO publication[5].

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

While 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.

7 Quality in testing

In procurement of condoms and regulatory monitoring, third party laboratories are widely used. Third party laboratories should be selected on the basis of their having certified quality management system (e.g. ISO 9001) or by their being accredited in accordance with ISO/IEC 17025 by a recognized body. Since compliance testing of condoms based on ISO 4074 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 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 programs. Accredited laboratories are periodically audited by national accreditation agencies.

8 Important parameters to be considered when using ISO 4074

8.1 Size

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 may cause problems in unrolling; one that is too large may 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 may have a market too small to be economical. Regulatory authorities or

buyers need to 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.

8.2 Resistance to breakage

It is necessary that condoms 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. The breakage of condoms may 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 comply with the requirements of ISO 4074 and should exceed 0,060 mm single wall thickness at mid-body.

8.3 Compatibility of materials

Oil-based “lubricants” often are easily available to users but should not be used with condoms. They degrade the latex film so quickly that the condom may fail during the period of normal use. This issue is dealt within ISO 4074 in the relevant section on labelling. The compatibility of the 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 8.7). Materials used in the manufacture of condoms including the foiling and packaging, should be proven to be compatible with the product by appropriate assessments during design and manufacturing stages.

8.4 Shelf-life and resistance to degradation

It needs to 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 of condoms are important for ensuring that the physical, performance and safety aspects of condoms are met throughout the claimed period. Only condoms properly formulated, 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. The condoms tend to undergo degradation by oxidation and decomposition of rubber polymer units. The condoms need to be stored protected from light, heat and mechanical damage so that the properties are not affected. Therefore it is recommended to protect the condoms by packing them in oxygen- and ozone-impermeable materials such as aluminium-foil laminates and to protect them from light-catalysed degradation reactions.

Shelf-life claims should be substantiated by well-designed stability studies, in accordance with Clause 7 of ISO 4074:2002. Shelf life should be determined by real time studies at $(30\ ^{+5}_{-2})\ ^{\circ}C$.

Clause 7 of ISO 4074:2002 defines the minimum stability requirement that needs to be complied with 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.

Since it is impracticable to complete real-time ageing studies before introducing products to the market, accelerated stability studies based on kinetic principles can be used to assign a provisional shelf life. Such provisional shelf lives assigned 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. There is no single method that has been sufficiently

validated or widely used to justify its designation as a standard method. Accelerated stability studies can be conducted by the methods described and referred to in Annex K of ISO 4074:2002 (which is not fully validated at the date of publication of this guidance document) 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 (refer to Technical Corrigendum to ISO 4074:2002) and time periods for accelerated stability studies needs to be made with caution as the application of this technique has only limited experience.

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

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

The following example illustrates the application of the time-temperature superposition technique described in Annex K of ISO 4074:2002 to accelerated ageing data obtained for a condom that has a poor reputation for ageing in real time. This method has not yet been demonstrated to be fully applicable for all types of condoms and is currently being reviewed by the relevant working group of ISO/TC 157.

EXAMPLE Time-temperature superposition plots were constructed from the accelerated ageing data according to the procedure described in Annex K of ISO 4074:2002. A value of 83 kJ/mol for the activation energy and a reference temperature of 30 °C were used to calculate the Arrhenius shift factors. The time-temperature superposition plot for bursting pressure times volume ($p \times V$) is shown in Figure 1. It can be seen that a reasonable degree of superposition has been obtained. The value of $p \times V$ after any proposed storage time can be estimated with a reasonable degree of confidence from this plot. For example, after 2 years at 30 °C the value of $p \times V$ will drop to approximately 50 kPa · l.

Figures 2 and 3, however, show that there is a poor degree of superposition for the pressure and volume curves. Nevertheless the following general trends can be seen.

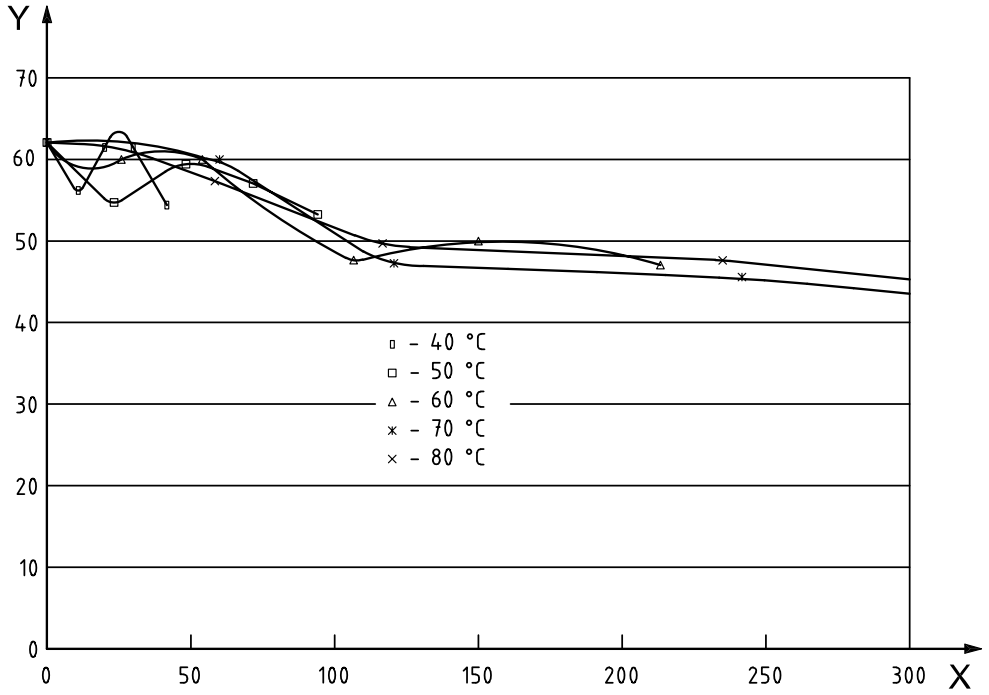
— The rate of decline in burst pressure versus transformed time reduces as the ageing temperature is lowered. This trend indicates that the burst pressure will be fairly stable at 30 °C.

— The rate of decline in burst volume versus transformed time increases as the ageing temperature is lowered. This trend suggests that burst volume changes will be more significant at 30 °C.

From Figure 2 it can be concluded that after 2 years at 30 °C, the burst pressure will be in the order of 2,2 kPa to 2,3 kPa. Given that the estimated value for the product of burst $p \times V$ after 2 years is 50 kPa · l, the burst volume will therefore be approximately 22 l. This value is fully consistent with the trend shown in Figure 3. With a burst volume of 22 l, taken together the distribution of burst volumes normally seen with this condom, compliance with the requirements of Clause 6 after 2 years at 30 °C is unlikely. We can conclude therefore that the shelf life of these condoms will be limited to approximately 2 years at 30 °C.

The Arrhenius shift factor between 30 °C and 50 °C for an activation energy of 83 kJ/mol is 7,7. Therefore the shelf life estimate can be confirmed by conditioning samples of the condom at 50 °C for 13,5 weeks (2 years/7,7) and assessing compliance with the burst property requirements defined in Clause 6. With this particular condom, it is clear that burst volume changes are more significant than burst pressure changes at lower temperatures. Studies to confirm shelf life should therefore be conducted at lower temperatures, such as 50 °C, rather than at high temperatures.

The data on stability testing shall be maintained as part of quality systems documentation and should be made available to regulatory agencies and purchasers when requested.

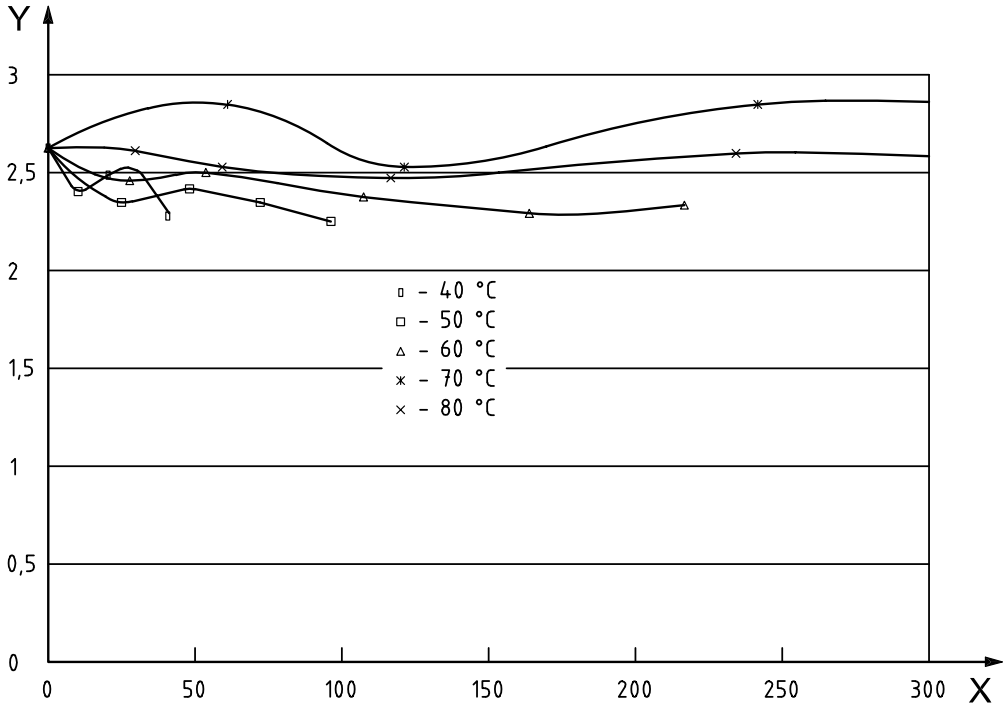


Key

X $p \times V$ (burst pressure $\times$ volume, kPa $\times$ l

Y time at 30 °C (weeks)

Figure 1 — Burst pressure times volume versus time transformed to 30 °C



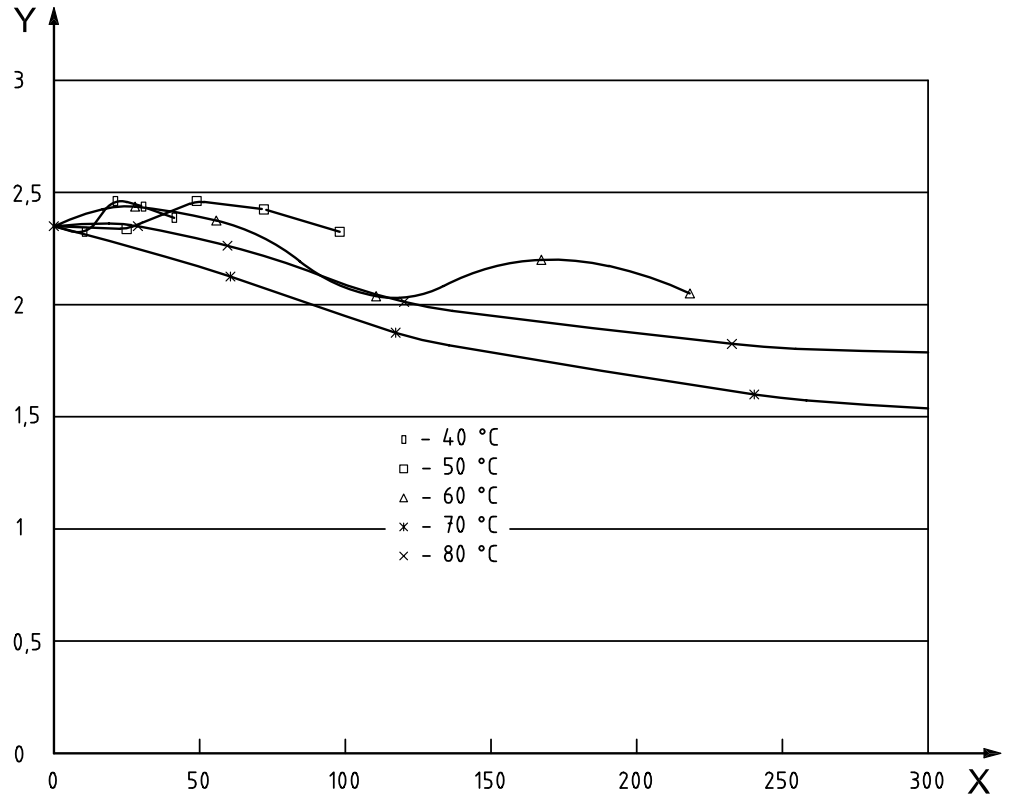
Key

X burst pressure, kPa

Y time at 30 °C (weeks)

Figure 2 — Burst pressure versus time transformed to 30 °C

8



Key

X burst volume

Y time at 30 °C (weeks)

Figure 3 — Burst volume versus time transformed to 30 °C

8.5 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 Clause 11 of ISO 4074:2002 and can be supplemented with special requirements of the purchaser and the regulatory agencies of each country.

8.6 Type testing

Type testing as referenced in Clause 7 of ISO 4074:2002 is used to establish the shelf life of the product. Data supporting the shelf life claim should be made available to regulatory bodies and purchasers on request. Type testing as referred to in ISO 4074 should not be confused with type test and type examination procedures required by some regulatory authorities, purchasers and validation procedures. Whenever there is any significant change to the formulation or process, the manufacturer should perform a new type test.

Examples of significant changes are change or addition of any new process chemical, change in packaging material for individually sealed containers, change in the leaching agent, dressing materials and type of lubricant.

Any changes in the formulation or process within previously validated ranges are not significant. The sample sizes and the tests to be carried out for type testing are specified in Annex B of ISO 4074:2002.

8.7 Lubricants

The lubricants used with the condom should be safe and compatible with rubber and chemicals used in formulation. The amount of lubricant is agreed upon by purchaser and is controlled as part of design control.

There are also condoms with lubricants containing spermicides and microbiocides, e.g. nonoxynol-9. Such lubricant attributes should be documented as part of design control.

9 Sampling

Condoms are medical devices and thus the manufacturer and the buyer need to understand sampling and set the parameters for acceptable quality. There is an absolute need to meet or exceed the minimum quality limits given in ISO 4074 and have an effective quality management system. The manufacturer can use any appropriate system to meet its quality objectives, but the sampling scheme set out in ISO 4074 and ISO 2859-1 are recommended when a lot is tested by a third party for compliance or for any other type of certification scheme. The use of smaller sample sizes can lead to a false assessment of the lot. It is of utmost importance that the samples are drawn randomly from the whole lot and randomised further before testing.

Bibliography

[1] ISO/TR 8550, *Guide for the selection of an acceptance sampling system, scheme or plan for inspection of discrete items in lots*

[2] ISO/TR 13425, *Guidelines for the selection of statistical methods in standardization and specification*

[3] ISO 2859-0, *Sampling procedures for inspection by attributes — Part 0: Introduction to the ISO 2859 attribute sampling system*

[4] ISO/TR 16142, *Medical devices — Guidance on the selection of standards in support of recognized essential principles of safety and performance of medical devices*

[5] WHO: Compendium on male latex condom

[6] ISO 9001:2000, *Quality management systems — Requirements*

[7] ISO 10993-1, *Biological evaluation of medical devices — Part 1: Evaluation and testing*

[8] ISO 13485:2003, *Medical devices — Quality management systems — Requirements for regulatory purposes*

[9] ISO 14971:2000, *Medical devices — Application of risk management to medical devices*

[10] ISO 16037:2002, *Rubber condoms for clinical trials — Measurement of physical properties*

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

[12] EN 455-3, *Medical gloves for single use — Part 3: Requirements and testing for biological evaluation*

[13] ASTM D5712-99, *Standard test method for the analysis of aqueous extractable protein in natural rubber and its products using the modified Lowry method*

[14] ASTM D6499-03, *Standard test method for the immunological measurement of antigenic protein in natural rubber and its products*

[15] BARKER, L.R. *J. Nat. Rubb. Res.*, **2** (4), 1987, pp. 210-213

[16] BARKER, L.R. *J. Nat. Rubb. Res.*, **5** (4), 1990, pp. 266-274

[17] GILLEN, K.T. *et al.* ISO/TC 157 WG 13 document, reference not given

[18] MANDEL, J. et al. *J. Res. Nat. Bur. Stand.*, 63C, **2**, Oct - Dec 1959

[19] GRIMM, W. *Drug Dev. And. Ind. Pharm.*, **19** (20), 1993, pp. 2795-2830

[20] PANNIKOTTU, A. and KARMARKAR, U. *Elastomer Service Life Prediction Symposium* '99, E.J. Thomas Hall, University of Akron