
Female condoms — Use of ISO 25841 and the quality management of female condoms

*Préservatifs féminins — Utilisation de l'ISO 25841 et du management
de la qualité des préservatifs féminins*

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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 Technical Reports 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 of 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 www.iso.org/iso/foreword.html.

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

Any feedback or questions on this document should be directed to the user's national standards body. A complete listing of these bodies can be found at www.iso.org/members.html.

Introduction

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

Female condoms that meet or exceed the requirements of ISO 25841 are effectively used for contraceptive purposes and in the prevention of sexually transmitted infections (STIs). They have adequate barrier properties, adequate physical properties so as not to break during use, are correctly packaged to protect them during storage throughout the claimed shelf life and are correctly labelled to facilitate their correct use.

ISO 25841 is a quality standard for female condoms, detailing the requirements for establishing the baseline specifications and for testing the finished product for compliance to the predefined specifications. It is applied by manufacturers, procurement agencies, regulatory bodies, and testing laboratories.

ISO 13485 is a generic standard for quality management of medical devices and serves as the requirement for regulatory compliance. The specific quality requirements for female condoms are given in ISO 25841. This document is a document providing manufacturers, buyers, regulatory agencies and third-party test laboratories, information relating to implementation and application of ISO 25841 and ISO 13485 in the quality management for manufacture of female condoms, and for purchasers to develop appropriate purchase technical specifications and to verify that condoms delivered comply with requirements of ISO 25841 and ISO 13485. This document outlines the importance of the requirements of the quality management system based on ISO 13485 that are applied during all the stages of design and development, production, supply, procurement, and post- production related to the complete life cycle of female condoms.

Consistent quality of female condoms, as other medical devices, is achieved by implementation of quality management system as per ISO 13485, which enables that quality is built into the product and assured at every phase in the design, planning, production, procurement processes and post-production activities. The requirements of ISO 13485 include implementation of the requirements ISO 14971 on risk management during all the phases of manufacture.

Female condoms, being medical devices, are subject to regulatory controls by national and regional regulatory agencies. The regulations address both the aspects of product approval and registration and licensing controls on the manufacture and distribution of female condoms. Compliance with the requirements of ISO 13485 and ISO 25841 are essential aspects which form the basis of regulatory approvals.

The specific additional requirements of buyers and consumers are specifically given due consideration when complying with the requirements of ISO 25841, as ISO 25841 is general by design, based on the designs that are currently approved for marketing. There are also specific documented technical specifications such as WHO UNFPA technical Specification on female condoms, which address the requirements of projects and procurement for public distribution programs.

The designs of female condoms, which are currently available in the market or under development, vary considerably with reference to the design of the sheath, the type of retention features, dressing materials, lubricants, etc. Thus, the failure modes of each design of female condom could vary significantly. Therefore, ISO 25841 requires that the efficacy and the safety of each design of female condoms should be substantiated by

- a) preclinical evaluations which would include standardization of physical properties, assessment of barrier properties, tests for stability and shelf life and assessment of biocompatibility to ensure the safety of materials that are used in the manufacture of female condoms and their components such as sheath, retention features, dressing materials, lubricants, additives, residual processing aids, etc. as prescribed in ISO 25841, and

- b) clinical investigations in humans to establish the efficacy and in vivo safety, as prescribed in ISO 25841, ISO 29943-2, ISO 10993-1, ISO 10993-5 and ISO 10993-10 and if necessary, ISO 10993-3.

Though female condoms are non-sterile medical devices, manufacturers are recommended to implement appropriate measures to minimize microbiological contamination of the product, by exercising controls on the components used in the manufacture of female condoms, manufacturing environment during manufacture of sheath, assembly of condoms and their packaging, manufacturing operations and health and hygiene of personnel.

It is important that properties of female condoms are maintained throughout the shelf life to ensure their safety and efficacy. ISO 25841 requires that the shelf life of any new or significantly modified female condom should be estimated by conducting stability studies as per ISO 25841 and, based on such studies, the appropriate storage conditions should be prescribed. The review of data of the shelf studies is important for granting product approvals and for awarding purchasing requirements.

This document also addresses how to deal with other important issues not directly covered by ISO 25841, but related to effective implementation of quality management system in manufacture of female condoms which will conform to the specifications of ISO 25841.

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Female condoms — Use of ISO 25841 and the quality management of female condoms

1 Scope

This document gives the essential principles in the application of ISO 25841. It outlines the details of elements applicable in quality management of female condoms as required by related normative standards, as referred in ISO 25841 and other relevant concepts.

This document supplements the use of ISO 25841 and addresses quality management aspects to be considered during the development, manufacture, quality verification and procurement of female condoms. It encompasses the principles of quality management systems in design, manufacture, and delivery of female condoms with emphasis on their performance, safety and reliability.

This document is applicable to female condoms made of natural rubber or synthetic rubber or synthetic polymers and the retention devices which form the integral components of female condoms.

NOTE Female condoms made from either natural rubber latex or synthetic rubber or other synthetic polymeric materials are addressed in ISO 25841.

2 Normative references

The following documents are referred to in the text in such a way that some or all of their content constitutes references for this document. For dated references, only the edition cited applies. For undated references, the latest edition of the referenced document (including any amendments) applies.

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

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

ISO 25841, *Female condoms — Requirements and test methods*

ISO 29943-2, *Condoms — Guidance on clinical studies — Part 2: Female condoms, clinical function studies based on self-reports*

3 Terms and definitions

For the purposes of this document, the terms and definitions given in ISO 2859-1, ISO 9000, ISO 13485, ISO 14971, ISO/IEC 17025, ISO 25841 and ISO 29943-2 apply.

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

- ISO Online browsing platform: available at <https://www.iso.org/obp>
- IEC Electropedia: available at <https://www.electropedia.org/>

4 Quality of design

4.1 General

Female condoms essentially comprise of the following components: sheath, which is made of natural rubber latex or synthetic rubber or other synthetic polymer material with an external retention device (retention feature) and where applicable, an internal retention device (product insertion feature). The dimensions of the barrier sheath and insertion features may vary depending on the proprietary designs, which have been validated for their safety and efficacy. The lubricant used in the female condoms also vary with the design of the manufacturers. Because of such a wide variety of the design and the materials, the unique features and characteristics specific design are detailed in the product Data sheet (see [4.5](#)).

The following features/characteristics have been listed in ISO 25841:

- a) product insertion into the vagina;
- b) product retention and prevention of slippage during sexual intercourse or penile removal;
- c) penile misdirection during sexual intercourse;
- d) invagination of the female condom during sexual intercourse;
- e) safe product removal after sexual intercourse;
- f) safety of all materials used in the construction of the female condom including the risk of any interaction between the materials;
- g) impermeability of the film to microorganisms;
- h) risk of breakage of the female condom during insertion, use and withdrawal.

4.2 Design input and design development

4.2.1 General

The requirements of design and development as prescribed in ISO 13485 are applicable in the design and development of female condoms. When the design and development activities relating to female condoms conform with the requirements of ISO 13485, the dimensions and shape of the female condoms and their components are appropriate for the anatomy and physiology of female and male reproductive organs and are proven to be functionally suitable for the efficacy of female condoms. Survey of clinical literature supported with laboratory scale development and evaluation of several prototypes enables that the female condom design fulfils the above criteria. Currently, several types of designs having shapes such as tubular, dome shaped, cylindrical, etc. with different types, material of construction and geometry of the external and internal retention features are available. The designs of the female condoms are not limited to the above and several innovative designs are under development. The designs of female condoms are mostly patented. While evaluating the options, it is important that the basis of evaluation takes into consideration the following potential failure modes listed in ISO 25841:

- 1) acute failure event;
- 2) clinical breakage;
- 3) non-clinical breakage;
- 4) total breakage;
- 5) clinical slippage;
- 6) clinical misdirection;

- 7) clinical invagination;
- 8) total clinical failure;
- 9) total female condom failure.

In addition to the given failure modes, other potential new failure modes which are identified during the risk assessment of design and development also play a vital role in development and validation of the design. It is quite possible that during the initial controlled clinical evaluations, additional information on the suitability of the designs will be available to be used for progressing further the development of the designs. Due to anthropometric variations of male and female reproductive organs, the optimal designs can have a range of dimensions and shape of the female condoms. The data sheets and labels of female condoms depict the essential features of dimensions and design of the specific type of female condoms.

Continual survey of technical information and reports on post-market clinical follow up and surveillance help keeping the design of the female condoms 'state-of-the-art' and minimize the risks of design and safety issues due any adverse events reported.

The design input delineates the required specifications including the details of materials used, process additives, residues that can potentially be left and the dimensions for the sheath, retention features, material, composition, and amount for the lubricant, dressing materials, details of packaging materials which is related to safe handling and storage of the female condom. The design input also includes the required physical strength and elasticity of the barrier sheath and the other components in the female condoms are appropriately built in them. While selecting the materials, due consideration is given to potential presence of residual accelerators, nitrosamines, monomers of materials used, residue of solvents used, degradation products generated during shelf life of female condoms and such other chemical residues which could have impact on the safety and biocompatibility. These evaluations also include properties of the materials of construction of retention features, any process additives such as mould releasing agents, washing solvent residues, etc.

A method for determination of nitrosamines is available in ISO 29941.

When female condoms are made of natural rubber latex, the potential of latex allergy is also considered and the manufacturing operations appropriately planned and implemented to reduce the potential of latex allergy.

4.2.2 Barrier sheath

The barrier sheath or pouch is made of materials established to be safe and nontoxic for use in inserted condition in contact with vaginal mucosal membrane. ISO 25841 requires that they should not liberate any toxic chemicals or leave any toxic residues during storage and use. The pouch is usually of tubular shape with the insertion features and retention features either attached to the sheath by fusing or as a free component, by assembling process after the sheaths are manufactured. The female condom, in the assembled form, is evaluated for compliance with the requirements of barrier properties according to [4.4.1](#).

4.2.3 Product insertion feature and retention feature

The insertion feature and retention feature may be produced by the manufacturer of female condoms themselves or procured from approved vendors under a well-defined technical agreement. The technical agreement covers the details of the material of construction such as:

- those of elastomers and open cell or closed cell sponges and design of these devices, which are currently being used;
- the evaluations of compatibility of the materials used with the barrier sheath and the lubricant which form the other integral parts of the female condoms;

- conformance with the requirements of biocompatibility evaluations as per ISO 10993-1, ISO 10993-5, ISO 10993-10, ISO 10993-23, and in addition ISO 10993-3, if necessary, when materials known for negative effects in genotoxicity, carcinogenicity and reproductive toxicity are used in exceptional cases if, for some reason.

During design and manufacture of these components, adequate consideration is given to ensure that the geometry and design of these devices are fit for the purpose and they do not cause any injury to the vaginal mucosa and skin of penis during use.

4.2.4 Dressing materials

The dressing powders are used essentially for providing a smooth surface and for avoiding stickiness of the condom during storage and use. The dressing materials that are used are selected based on the physical and chemical compatibility with the components of female condoms and overall biocompatibility evaluation requirements of female condoms.

4.2.5 Lubricants

The female condoms contain lubricants which are chemically compatible with the other components of the female condoms and comply with requirements of biocompatibility evaluations. Since the surface area of female condoms is much larger than that of male condoms, the quantity of lubricant to cover the entire surface of female condoms is much higher. The material and grade of the material such as viscosity are important considerations that go in the selection of lubricant for female condoms. The quantity of lubricant used varies for each design of female condoms. The ability of the lubricant to migrate and cover the entire surface of the female condoms is also considered in the evaluation of the lubricants.

During the use of female condoms, the need for additional lubricants may become necessary. The additional lubricant may be supplied as companion sachet packs in a composite pack, by the manufacturer of female condoms. In some cases, the use of stand-alone personal lubricants is also recommended. The development of the design of female condoms includes the evaluation of compatibility of such additional lubricants with the female condoms before including or recommending them for use with the female condoms.

4.2.6 Biocompatibility

While designing the female condoms, the requirements of ISO 25841 for biocompatibility evaluation for the female condoms and their components such as barrier sheath, insertion features, dressing materials, lubricants, pigments and fragrances, if used, are considered and ensured that they are complied with.

4.2.7 Control of bioburden

The female condoms are nonsterile medical devices. However, since they come in contact with vaginal mucosa and outer skin of penis, in order to minimize the potential of infection, it is essential that they do not contain excessive microbial population and are free from pathogenic microbes such as *Staphylococcus aureus*, *Pseudomonas aeruginosa* and *Enterobacteriaceae*, including *Escherichia coli*. ISO 25841 recommends that the manufacturers control the total viable microbial counts and ensure the absence of specific pathogens as above. In order to achieve this, manufacturers consider the bioburden control aspects in the design and manufacturing stages. Some of the dressing materials such as starch can be a good medium for proliferation of microbes. The assembly of female condom sheath with the retention features is done usually by manual operation. Implementation of appropriate control measures enable controlling the bioburden potentially caused by manual operation. Additional details are given in [Clause 6](#).

4.2.8 Packaging

The material and construction of individual containers are designed such that containers offer adequate protection against mechanical damage, oxidation, direct sunlight, and excessive humidity

(where applicable) to the female condom, which is packed in it. The composition and structure of laminates used for packing the female condoms in individual container ensure that the stability of the female condoms is maintained throughout the labelled shelf life, when stored at the prescribed storage conditions. Since the female condom is quite bulky in size and contains more quantity of lubricants, in comparison to male condom, the design of an individual container includes additional considerations to provide effective sealing to comply with the requirements of ISO 25841 with respect to visibly open seals and package seal integrity. The labelling requirements, according to ISO 25841, are also the factors which are considered in design and determination of the size of the individual containers appropriate to include the required labelling matter in legible form.

4.3 Design verification

The verification of the design performed in the prototype designs includes verification of physical and chemical properties, safety, biocompatibility evaluations, clinical performance evaluations and stability evaluations. The methods used for these verifications may involve specific instruments, as detailed in the data sheet to ensure conformance with the requirements as given in ISO 25841. The properties and attributes that are verified include verification of mechanical strength and elasticity, measured in terms of burst volume and burst pressure of the female condom design. The limits of burst volume and burst pressure are arrived at specifically for each design, based on the samples used for clinical studies which were proven to comply with the requirements of clinical investigations, as described in 4.4.2. Other parameters such as tensile properties may also be included in the design verification. It is also important to verify the physical properties of the retention features in terms of their dimensions, freedom from deformation of shape, hardness, stiffness (modulus), density and firmness of fixing of retention features, as applicable. Shelf-life estimation and stability evaluations are carried out as part of design verification. Adequacy of measures prescribed for control of bioburden as per ISO 25841 are also verified.

4.4 Design validation

4.4.1 Evaluation of barrier properties

The efficacy of the barrier properties of the film and the new design of female condom and if significant change(s) is made is established by evaluation of barrier properties as described in ISO 25841:2017, Annex H. Bacteriophage Phi- X174 is used as surrogate for evaluating the resistance to permeability of viruses and other microorganisms and spermatozoa for fulfilling the requirement of the contraceptive and STI prophylactic barrier properties. ISO 25841 provides for other test substances to be used, provided that such test substance is validated to be equivalent to the specified bacteriophage in simulating the permeability parameters.

4.4.2 Clinical (human use) investigations

ISO 25841 prescribes the following requirements for the validation of any new design of female condom and if significant change(s) is made:

- a) clinical effectiveness study for pregnancy rate evaluation;
- b) extrapolation from clinical effectiveness study of already approved female condom. If the design and specification of new female condom are sufficiently like those of a marketed device and that marketed device has a known pregnancy rate established from a clinical effectiveness study, then the manufacturer may refer to the estimated pregnancy rate of the marketed device instead of conducting a contraceptive effectiveness study on the new device. The requirements of selection of the control condoms are given in ISO 25841.

4.4.3 Stability studies and shelf-life claim

The shelf-life claim of the female condoms is validated by conducting stability studies according to ISO 25841, on female condoms that have been stored for the maximum validated period in unfoiled condition. The stability studies are conducted on samples from minimum three lots of fully assembled

female condoms with their retention features, lubricated and packed in the individual containers. The stability studies cover the minimum stability studies before placing the designs of female condoms in the market, accelerated stability studies to estimate the shelf life and provisionally assign the shelf life pending real time stability studies and real time stability studies to substantiate the shelf-life claim. The real-time stability studies are conducted at temperature of $(30 \pm \frac{2}{5})$ °C. The outcome of the studies thus conducted support the claimed shelf life of the female condoms when stored up to a mean kinetic temperature of 30 °C. This is to cover the storage and distribution conditions that can practically be achieved in female condom supply chain. Some of the designs of female condoms may be made of materials that can be sensitive to variations in levels of humidity during packing, shipping, and storage. In such cases, stability studies include controlled temperature and humidity conditions. The guidelines of the International Council for Harmonisation (ICH) [International Medical Device Regulators Forum (IMDRF)] for conducting stability studies for pharmaceuticals for climatic condition Zone IVb are followed for conducting stability of such designs.

4.5 Design output

4.5.1 General

The design output established and signed off based on the specifications and parameters arrived at as per the design and development activities described above forms an essential part of documentation of Design History File.

The specification details pertaining to the female condom that should be documented in Data sheet are given in ISO 25841:2017, Clause 16. The content of design output essentially includes, but are not limited to, the following details.

4.5.2 Details of materials

- a) Specifications and test methods of the materials used for the barrier sheath, retention features, dressing materials, lubricant, primary packing material used in individual container, pigments and fragrances, if used.
- b) Their material safety data sheets; storage conditions and handling conditions.
- c) Requirements of retesting based on their shelf life.

4.5.3 Specifications of the female condoms

- a) Technical drawings showing geometry and dimensions of female condom and retention features and correct locations of fixed retention features.
- b) Specifications for length, width and thickness, the points at which they are measured.
- c) Type and amount of lubricant and dressing powder.
- d) Specifications for bursting volume and bursting pressure as calculated based on the clinical trials, according to ISO 25841:2017, 11.1.
- e) Test methods and results for retention features.
- f) Conformance to all the specifications detailed in ISO 25841 as part of Quality Verification. Details of any deviations from the test procedures and/or requirements specified in in ISO 25841. Such deviations are justified in the data sheet. Examples include the quantity of water that to be used in the test for freedom from holes.
- g) Labelling requirements to ensure compliance with the requirements of ISO 25841 and applicable national and regional regulatory requirements.
- h) The basis of assigning date of manufacture and expiry date, based on the stability studies.

- i) If additional lubricants are supplied along with female condom in the composite pack, the expiry period of the lubricant and female condom and the earliest of them will be labelled on the composite pack.
- k) Storage and handling conditions for the intermediates, work in progress and finished product at the manufacturer's site.

4.5.4 Supporting information

- a) Summary of supporting details relating to biocompatibility evaluation, clinical studies and stability studies.
- b) In-process tests that are performed at the stages of manufacture, quality plan and corresponding acceptance criteria.

4.5.5 Regulatory compliance

The details that are required to be submitted as prescribed for regulatory compliance and product approval.

4.6 Design transfer

The design transfer carried out on the validated design of the female condom are supported with documented protocol and reports.

Applicable process validations are carried out for each stage of manufacture viz. Dipping or moulding, electronic testing, assembly, packing in individual containers and subsequent stages of packing. Scale up validations and production scale validations performed documented establish the required process capability of largescale production of female condoms. The validations demonstrate successful compliance with the predefined specifications consistently on minimum of three production scale lots/batches.

Since the testing of female condoms involve special equipment and or modifications to equipment used for testing male condoms, the design transfer activities include as part of compliance with the requirements of ISO 13485 and ISO 25841, the additional details of testing procedures and equipment.

4.7 Validation and change controls

Whenever significant changes are made to the formulation, dimensions or process that can substantially affect the performance and/or safety of the condoms, such changes are duly evaluated, validated and documented [e.g. changes in types of materials and formulation; changes in dimensions; changes in lubricant; changes in primary (individual) packaging material; changes in dipping, moulding, leaching, electronic testing and foiling and packing processes; changes in sources from where critical components such sheath, retention features, primary packing materials are procured]. Significant change is described as any change carried out to the approved design or process with the scope to materials included packaging, formulation, manufacturing process, facilities or equipment which might impact on the performance, intended use, shelf life or any other safety aspects, which cannot be clearly excluded by a risk analysis.

Periodic revalidation performed on design and processes addresses the impact of cumulative minor changes, changes in regulatory requirements, changes in materials used and changes and improvements in manufacturing technology.

5 Risk management

Risk management carried out according to the requirements of ISO 14971 encompasses the total life cycle of female condom, starting from design development, manufacture, storage and shipping, use and post-use aspects.

The risk associated with materials of construction and design are very important and the risks associated with potential failure modes are of great significance, especially considering the complexities involved related to usage of condoms.

The risks associated at each stage are analysed, evaluated, and controlled such that residual risk is at acceptable level. Any residual risk, which can be mitigated by appropriate communication to user, is achieved by documenting them in labelling of female condoms (e.g. latex allergy) and provision of information on the packs and leaflet to users. As a measure of continuous improvement, the level of acceptable risk is continually improved by application of developments in science, technology, and clinical usage. The independent review and interpretation of design development, manufacture, usage, and feedback from post market follow up support in providing the basis of strong and well-established principles of clinical studies, state of the art and technology and statistics. Any new risks arising out of large-scale use of female condoms captured through planned arrangements are analysed and remedial measures implemented. Field safety corrective actions and advisory notes that are issued based on post-marketing surveillance, customer complaint analysis, regulatory advices, developments in knowledge provide continual basis for implementation of appropriate follow up actions.

Planned arrangements implemented to perform risk analysis at periodic intervals and risks managed adequately with appropriate follow up actions ensure continued suitability and effectiveness of quality management systems associated with female condoms.

When required by regulatory agencies and procurement agencies, the risk management report is submitted by the manufacturer.

6 Quality in manufacture

Manufacture of female condoms (including design and development) is carried out by organizations, in which the conformance with the requirements of ISO 13485, principles of good manufacturing practices for medical devices, as applicable are implemented and documented. The manufacture of female condoms is conducted in dedicated facility appropriately constructed and maintained for manufacture of medical devices. This also ensures that the female condoms are manufactured in site without potential of cross contamination from any hazardous and poisonous materials.

Adequate and appropriate resources in terms of quality management system, infrastructure, manufacturing and storage spaces, environmental conditions, suitably competent, qualified, and trained personnel; equipment for manufacturing and testing are provided and implemented.

The input materials and components are procured from only the approved vendors, as per the purchase specification arrived at based on the design output and validation. For critical components such as retention features, in addition to the purchase specification, a detailed technical agreement is recommended to be drawn between their manufacturers and the manufacturer of female condom.

The manufacturers of female condoms implement adequate bioburden control measures encompassing air handling system, lay out and fabric of the building, cleaning and sanitization activities, personnel health and hygiene, packing materials used in storage of incoming materials and work in progress, cleaning and sanitization of components used and machines. Bioburden is addressed as part of risk analysis and periodic monitoring of bioburden is carried out. The manufacture consisting of steps such as dipping, moulding, welding, electronic testing, assembly, storage of work in progress and packing are carried out in environment with control on bioburden with appropriate sanitation and hygiene conditions and personnel control. The results are reviewed, and appropriate corrective actions taken when alert and action limits are exceeded and out of trend results are observed.

Provision of adequate infrastructure for carrying out the manufacturing operations and well-designed lay out of the premises facilitate orderly movement of materials and personnel and location of manufacturing operations in sequence. The potential mix ups of products and materials and congestion of storage areas are avoided. Potential contamination into the manufacturing and storage areas are controlled by implementing effective rodent and pest control measures.

When software systems are used for manufacturing, quality control and document control activities, they are designed and validated such that adequate controls are implemented on the accuracy and security of creation, access and modification of data and their storage. Maintenance of back up of data and documents, preferably at an offsite location ensure business process continuity in the event of unforeseen damage / disruption in the manufacturing facility.

Well-planned and implemented training activities which include the training on the relevant standards such as ISO 25841, ISO 13485, ISO 14971 and good manufacturing practices, on the job technical training; training on applicable procedures and work instructions, training on safety and human resources development topics as a part of quality management, the effectiveness of training and competence of personnel are monitored by appropriate evaluation and assessment by implementing well planned schedules.

For the implementation of effective quality management system, the essential components are:

- use of equipment that are qualified and appropriately calibrated;
- adequately trained personnel whose competence are periodically verified;
- the manufacturing operations and testing activities which are carried out based on validated procedures;
- planned quality verification activities;
- nonconformances which are duly investigated and controlled followed up with appropriate corrective and preventive actions; and
- activities and data which are recorded as applicable.

The manufacture of female condoms involves some manual and semi-automated operations such as assembly of retention features, dosing of lubricant, packing in primary container, etc., the effectiveness with which of such operations are carried out is periodically assessed and when required, appropriate retraining of the operators carried out.

The qualified manufacturing equipment and machinery for the operations and are maintained as per planned maintenance schedules. The selection of components of the equipment and processing operations takes into consideration that they do not lead to contamination of the materials that are being processed. The equipment is cleaned after operation by validated cleaning procedures to ensure effectiveness of cleaning and absence of residues of cleaning materials and materials previously processed in them.

If any of the process stages are subjected to reprocessing as a result of outcome of in-process QC testing, for such reprocessing operations appropriate additional validation and evaluation of additional risks that would be posed by such reprocessing activities are implemented.

Female 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 female condom manufacturers strive to keep the latex-protein level minimal. Control of extractable proteins is a quality management aspect and the manufacturers control the content and release of allergenic substances, such as extractable proteins, by appropriate process steps and controls. The methods for determining protein levels in latex products are given in ASTM D5712-99 and EN 455-3.

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

No limits for protein levels have been established in ISO 25841.

The composition of the lots of female condoms is carried out in compliance with the ISO 25841, ensuring homogeneity of the components that go in for the composing the lot. Identification and traceability of components and materials used are maintained, encompassing all the stages of manufacturing of the sheath, assembly of the female condom and lubrication and packing. The reconciliation of materials

used is carried out for each lot of the finished product of female condoms. Any abnormal deviations are investigated and resolved before the release of the product for distribution.

It is important that the inspection and test status of the materials is maintained in all stages of manufacture and dedicated spaces according to lot wise and inspection status wise segregation are used for the storage of work in progress and finished products.

The process capability of manufacturing operations, monitored by appropriate statistical process control tools such as Schewhart charts, CUSUM, etc. enable timely detection of deviations and implementation of appropriate on course corrections and adjustments made to the processing conditions to ensure the quality of the products and optimization of production operations. In-process challenge tests for assessing the efficacy of electronic testing activity and sealing and packing activities are carried out at periodic intervals as per documented work instructions and quality plan.

The storage and distribution activities are carried out according to documented procedures and applicable records maintained. ISO 25841 requires that the storage of female condoms and the work in progress be under controlled conditions with maximum temperature of 30 °C. Temperature profiling and temperature records of warehouses and production areas provide documentary support that the prescribed storage conditions are maintained to demonstrate addressing these aspects.

The data and document control activities include control and effective management of data accuracy, safety and storage and retrieval for prescribed period of time. The device manufacturing record (DHR) and the representative sample of each lot of finished products, adequate to carry out at least one set of complete testing are stored for a period as prescribed by national and regional regulatory authorities or for the labelled shelf life and 6 months beyond.

It is possible that some stages of manufacture of female condoms such as sheath forming, assembly, packing of finished goods, storage of products, etc. may be outsourced. The manufacturer of the female condom is ultimately responsible to ensure that the subcontractors comply with all the regulatory requirements, QMS requirements, technical requirements, and conformance to prescribed specification. A detailed technical agreement is implemented which will clearly delineate the responsibilities of the manufacturer and subcontractor and the joint responsibilities.

The quality management aspects of post-production stages include monitoring of shipping and transport conditions, post market surveillance, customer feedback surveys, customer complaints and product recalls, if warranted, continual review and updating of relevant technical and regulatory requirements and published technical information.

Appropriate follow up actions are implemented at relevant stages of design, development and manufacture of female condoms.

Appropriate systems are implemented for control of nonconformance, corrective and preventive actions, handling of customer complaints and self-inspection as prescribed by ISO 13485.

7 Quality in testing

7.1 General

To achieve conformance of finished products to the specifications of ISO 25841, a well- defined and documented quality plan covering all the stages of manufacture from control of input materials such as raw materials; packaging materials; components and intermediates; and the finished products, is implemented. The quality plans give details of stages, sampling levels, tests to be performed, Accept/Reject criteria, test method to be followed and documentation of test results. The sampling plan for the finished product is given in ISO 25841. The sampling plans for receiving inspection and in-process quality control are defined based on the process capability of the manufacturing operations and suppliers' capabilities to conform to the specifications of materials supplied by them. The sampling plans are based on sound statistical basis and application of requirements of ISO 2859-1.