

Annex 11

World Health Organization/United Nations Population Fund specifications for plain lubricants

Background

The report of the Fifty-third meeting of the World Health Organization (WHO) Expert Committee on Specifications for Pharmaceutical Preparations (ECSP) in 2018 (1) stated the following:

Ms Seloi Mogatle and Dr William Potter from the United Nations Population Fund (UNFPA) gave an update on the prequalification guidance for contraceptive devices and condoms. The UNFPA had contacted WHO to inquire how best to start a process to update the relevant texts that were adopted by the ECSP and published in 2008 (2, 3). The Expert Committee agreed to the importance of updating these materials in view of the changes in the contraceptive field globally over the previous decade. The two organizations committed to work together to bring the documents up to date. It was suggested by UNFPA to separate out the current existing procedure for condoms to include the following aspects:

- 1. prequalification guidance for contraceptive devices;*
- 2. prequalification programme for male latex condom and annexes;*
- 3. technical specification for male latex condom and annexes;*
- 4. male latex condom prequalification inspection aide memoire;*
- 5. condom quality assurance and annexes;*
- 6. guidance on testing male latex condoms;*
- 7. condom storage and transportation;*
- 8. post-market surveillance of condoms;*
- 9. public assessment reports for contraceptive devices – condoms and intrauterine devices.*

UNFPA also raised the issue of specifications for lubricants (both water-based and silicon-based), which needs to be considered when developing the new guidelines.

The Expert Committee supported the development of the relevant documents for prequalification of condoms in consultation with the WHO

Secretariat and their preparation for public consultation and took note that they will be reported back to the Expert Committee.

As agreed at the ECSPP meeting in October 2018, UNFPA and WHO have separated out different aspects of the current procedure for contraceptive devices and condoms.

All related documents were restructured and revised in the first half of 2019, then sent out for public consultation in July 2019. Comments received were reviewed by a group of specialists in October 2019, before being presented to the ECSPP. This is one of the three adopted by the Fifty-fourth ECSPP meeting to replace the previous guidance document.

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1. Introduction

The following guidelines give the specifications for procurement of additional lubricants to be used with male and female condoms in reproductive health programmes.

These guidelines have been updated following a detailed technical review conducted at the United Nations Population Fund (UNFPA) Global Consultation on Lubricants in November 2016 in Bangkok, Thailand, and a follow-up meeting, primarily with lubricant manufacturers, held in conjunction the Thirty-fourth ISO/TC 157 (International Organization for Standardization, Technical Committee 157 for Non-Systemic Contraceptives and STI Barrier Prophylactics) meeting in George Town, Penang, Malaysia in September 2017.

The Global Consultation on Personal Lubricants was convened to review the safety of personal lubricants, as research has shown users may experience irritation, burning and damaging effects to vaginal and rectal tissue, and to examine the ways to produce, procure and distribute safer products for all. Hosted by UNFPA, the United States Agency for International Development (USAID), the World Health Organization (WHO) and the International Planned Parenthood Federation (IPPF), the meeting brought together more than 80 manufacturers, researchers and technical experts, sexual health advocates and educators, as well as international organizations that procure lubricants for governments or local organizations.

The status of the WHO/UNFPA/FHI360 (Family Health International) advisory note on *Use and procurement of additional lubricants for male and female condoms* published in 2012 (4), was also reviewed at the Global Consultation. It was agreed that the majority of the recommendations made in that note are still valid and they have been incorporated in this specification. The recommendation that polyquaternary compounds should be avoided was found to be no longer supportable and has not been included in this specification.

2. Requirements

Manufacturers shall include in their product dossier evidence to confirm that the lubricant complies with the requirements listed in [Table A11.1](#). Verification of conformance to these requirements is assessed by review of the product dossier.

Table A11.1
Generic requirements

Requirements	Description
<p>Definition and general properties</p>	<p>Description</p> <p>Water-based lubricants shall be clear, translucent or white gels or viscous liquids. They shall be free from lumps and foreign matter and be non-staining and water washable.</p> <p>Silicone lubricants shall be clear, translucent or white gels or viscous liquids free from lumps and foreign matter and be non-staining.</p> <p>Ingredients</p> <p>Lubricants shall contain only ingredients that are safe for human use in contact with vaginal mucosa and skin during sexual intercourse. The ingredients shall be non-irritant and non-toxic and shall not liberate any toxic or harmful substance during storage and use.</p> <p>Lubricants shall be free from added fragrance, colour, spermicides, herbal ingredients and special ingredients that claim specific pleasure-enhancing properties.</p> <p>Silicone lubricants shall contain a minimum of 30% polydimethylsiloxane (dimethicone), with a viscosity of 5 cps (centipoise) and above (mixtures of polydimethylsiloxanes with different viscosities are permitted).</p> <p>Compatibility with condoms</p> <p>Lubricants shall be compatible with male and female condoms (any exceptions shall be noted in the labelling). Testing shall be conducted according to ASTM D7661 (5) and ISO 19671:2018 (6). When testing silicone lubricants containing volatile cyclomethicone, the conditioning of the condoms in the presence of the lubricants should be done under occlusive conditions, to prevent evaporative loss of the cyclomethicone.</p> <p>Preservatives</p> <p>Water-based lubricants shall be preserved against microbial contamination and shall contain suitable preservatives. The lubricant shall be manufactured under suitable conditions, to maintain control of bioburden.</p> <p>Sterility</p> <p>Lubricants may be supplied sterile in unit-dose containers.</p>

Table A11.1 *continued*

Requirements	Description
	<p>Manufacturer</p> <p>Lubricant shall be manufactured in accordance with certified quality management systems (QMS) and in compliance with national and regional regulatory requirements. The QMS shall comply with ISO 13485 (7). Lubricant shall have regulatory approval such as a CE Mark or United States Food and Drug Administration (US FDA) 510(k) clearance (8).</p> <p>Lubricity</p> <p>There are currently no specification requirements for lubricity, nor are there any recommended methods for measuring lubricity. Manufacturers who specify lubricity requirements should submit details of the specification and test method to UNFPA. Similarly, manufacturers who test for the retention of lubricity over the time of use should submit details of the test method and requirement.</p>
Composition	<p>The manufacturer shall submit to procurement agencies full composition details of the lubricant, with the quantities and specifications of individual ingredients used. Wherever available, the ingredients shall comply with corresponding pharmacopoeia specifications. When specific proprietary ingredients are used, their material safety information shall be submitted.</p> <p>Water-based lubricants shall be formulated to comply with the requirements listed next.</p> <ul style="list-style-type: none"> • Osmolality shall be less than 1200 mOsm/kg.¹ This osmolality limit can be achieved by keeping the total glycol content below about 8.3 mass fraction (%w/w).² • pH shall be in the range 5.0 to 7.0.³ • Viscosity shall be within the tolerance of $\pm 10\%$ of the value specified by the manufacturer. The manufacturer shall submit the method of determination of viscosity, giving details of equipment, temperature conditions, spindle speed, spindle number and shear rate. <p>Silicon-based lubricants shall be formulated to comply with the requirements listed next.</p>

¹ This requirement is under review and might be revised at a future date.

² This limit may be varied depending on the specific glycols used.

³ Note: Lubricants with a low buffering capacity that do not disturb the pH of the vagina or rectum are preferred.

Table A11.1 *continued*

Requirements	Description
	<ul style="list-style-type: none"> • Viscosity shall be within a tolerance of $\pm 10\%$ of the value specified by the manufacturer. The manufacturer shall submit the method of determination of viscosity, giving details of equipment, temperature conditions, spindle speed, spindle number and shear rate.
Biocompatibility	<p>Lubricants shall comply with the requirements of biocompatibility assessments conducted in accordance with ISO 10993-1 (9), for specific parameters of cytotoxicity (ISO 10993-5) (10) and skin irritation and sensitization (ISO 10993-10) (11).⁴ The toxicity study reports shall be reviewed and interpreted by a qualified toxicologist or other suitably qualified expert. Full reports of biocompatibility assessments shall be submitted as part of the product dossier.</p>
Bioburden levels	<p>Lubricants need not be sterile. However, they shall be subjected to control of microbial contamination by appropriate measures taken in formulation, manufacturing and packing operations. In the finished product, bioburden levels shall be maintained below 100 cfu (colony-forming units) per gram (USP 1111) (12). There shall be an absence of <i>Pseudomonas aeruginosa</i>, <i>Staphylococcus aureus</i>, <i>Candida albicans</i> and <i>Escherichia coli</i>. These requirements apply to both water-based and silicone-based lubricants.</p> <p>Bioburden levels shall be maintained at the above levels during storage and repeated opening of a container during multiple use.</p> <p>Lubricants shall comply with the evaluation of preservative efficacy, performed as per the requirements of a relevant pharmacopoeia.</p> <p>If the lubricant is supplied sterile in unit-dose containers, the sterility assurance level shall be 10^{-6}.</p>

⁴ Note: Some regulatory authorities require acute systemic toxicity to be assessed. For example, USFDA requires acute toxicity testing by intraperitoneal administration.

Table A11.1 *continued*

Requirements	Description
Shelf-life and stability	<p>Lubricants shall have a minimum shelf-life of 3 years from the date of manufacture.</p> <p>To ensure compatibility with condom-storage recommendations and shelf-life estimates, real-time studies shall be conducted within the temperature range of 28 °C to 35 °C. The humidity shall be maintained at (75 ± 5%) relative humidity (RH), to ensure conformity with Zone IVb (hot, higher humidity) requirements.</p> <p>In line with International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) guideline Q1A(R2) (13), accelerated studies shall be conducted at 40 ± 2 °C and 75 ± 5% RH. Manufacturers may elect to use higher temperatures such as 50 °C and 60 °C, providing the results can be correlated with real-time shelf-life estimates at 28 °C to 35 °C.</p> <p>For water-based lubricants, manufacturers should include freeze/thaw cycling in their stability studies, to confirm that the lubricants can tolerate freezing. Manufacturers should also confirm that osmolality remains within specifications at the end of the stability study and undertake intermediate osmolality measurement if any significant changes occur to the water content and/or viscosity of the lubricant, and, in the case of lubricants packed in sachets, the weight of the sachets during the course of the study.</p> <p>Critical parameters, including pH, bioburden, viscosity, odour, physical condition, etc., shall be monitored during stability studies. For water-based lubricants, preservative assays and microbiological challenge tests shall be conducted during stability studies. Silicone lubricants containing cyclomethicone should be monitored for weight loss due to any loss of volatile material through the packaging.</p> <p>Lubricants shall remain within the manufacturer's specification for the duration of the shelf-life period.</p> <p>The data and report on accelerated stability studies and ongoing real-time studies shall be submitted as part of the product dossier.</p>

Table A11.1 *continued*

Requirements	Description
Compatibility with condoms	<p>The manufacturer should submit reports of compatibility studies conducted on the use of lubricant with male and female condoms made from natural rubber latex and synthetic materials. The toxicity study reports shall be reviewed and interpreted by an appropriately qualified person to assess toxicology reports, e.g. a pharmacologist, pharmacist, microbiologist or a laboratory medicine specialist.</p> <p>If any biocompatibility or toxicity risks are identified, a risk/benefit analysis shall be included in the report. Full reports of biocompatibility assessments shall be submitted as part of the product dossier</p> <p>Any exceptions from testing or incompatibilities shall be noted.</p>
Packaging	<p>Individual containers</p> <p>Lubricants shall be packed in tamper-evident containers that facilitate multiple delivery of lubricant. Examples are collapsible/squeeze tubes and containers with a suitable delivery system for application of lubricant.</p> <p>It is recommended that containers should be made of recyclable materials that are compatible with the lubricant, as substantiated by stability studies and shelf-life claims. The containers shall not have sharp edges. They shall not liberate any toxic or harmful substance during storage and use of the product. The individual containers shall be free from leakage of lubricant.</p> <p>The recommended nominal contents for multi-dose containers are 35 g, 50 g and 82 g. Other sizes may be considered, depending upon programme requirements. The recommended nominal contents for a single-dose sachet is 3 g for silicone lubricants and 4–5 g for water-based lubricants.</p> <p>Pack contents are based on the amount of lubricant that can be expressed from the pack under normal use. This will be evaluated by weighing 20 full primary containers individually and weighing them again after squeezing out their contents. Alternatively, the weight of lubricant expressed may be determined directly by collecting it in a tared container or dish.</p>

Table A11.1 *continued*

Requirements	Description
	<p>Secondary packing</p> <p>The individual containers shall be packed in secondary distribution packages of an appropriate size as per programme requirements (e.g. 25 units per secondary pack).</p> <p>Cardboard boxes shall be Forest Stewardship Council (FSC; or equivalent) marked/certified. They shall only contain paper/cardboard. Plastic coating shall not be used.</p> <p>Shipper cartons</p> <p>Shipper cartons shall be FSC (or equivalent) marked/certified. They shall be made of a minimum of 40% recycled/post-consumer material.</p> <p>The shipper carton should only contain paper/cardboard. Plastic coating shall not be used.</p> <p>By 2020, the plastic carton liner shall be made from recycled material/plastic and biodegradable plastic.</p> <p>The recommendations relating to packaging in this specification may be varied depending on the intended use of the lubricant. Full details of the required packaging should be agreed in advance and specified in purchase orders.</p>
Labelling	<p>Individual containers</p> <p>Labelling requirements may be subject to local regulatory requirements. Subject to any local requirements, the individual containers shall be marked with the details listed next.</p> <ul style="list-style-type: none"> • Contents (specify if it is water- or silicone-based lubricant) • The quantity of lubricant that can be expressed from the container in normal use • If in a multi-dose container, advice on the amount of lubricant to be used • Manufacturer's name and address • Batch/lot number • Expiry date (in YYYY-MM format) • Storage conditions – store at an average temperature below 30 °C and avoid exposure to direct sunlight • Warnings/special notes, if any • Maximum time period in which the contents can be used after the container was first opened • A list of any ingredients that may be an irritant or that could cause allergic reactions

Table A11.1 *continued*

Requirements	Description
	<ul style="list-style-type: none"> • A statement that the lubricant is compatible with male and female condoms (any exceptions, such as male polyurethane condoms, shall be stated on the package) • A statement that lubricant is not a contraceptive and does not protect against pregnancy, sexually transmitted infections and HIV. To protect against pregnancy and sexually transmitted infections, the lubricant must be used with a condom. <p>Secondary packaging</p> <ul style="list-style-type: none"> • Contents • Quantity • Manufacturer's name and address • Batch/lot number • Date of manufacture and expiry date (in YYYY-MM format) • Storage conditions • Warnings/special notes, if any <p>Shipper cartons (or as per UNFPA shipping instructions to be provided by the buyer)</p> <ul style="list-style-type: none"> • UNFPA logo • UNFPA project number • UNFPA purchase order (PO) number • Country of destination • Contents as water-based lubricants • Quantity • Manufacturer's name and address • Batch/lot number • Date of manufacture (in YYYY-MM format) • Expiry date (in YYYY-MM format) • Weight • Volume • Storage conditions text: "Store in well-ventilated, dry storage conditions with an average temperature of less than 30 °C away from direct sources of heat including sunlight" • Warnings/special notes, if any, to be defined by the manufacturer • Any special shipping instructions defined by the manufacturer

2.1 Lot-by-lot testing requirements

The manufacturer shall submit a certificate of analysis for each batch/lot of lubricant supplied, confirming conformance to the requirements specified in this section. This section may also be used by accredited/approved laboratories for the independent testing of lubricants.

Parameter	Requirements	Verification
Description	<p>Water-based lubricant shall be clear, translucent or white gel or viscous liquid, free from lumps and foreign matter, and water washable.</p> <p>Silicone lubricants shall be clear, translucent or white gels or viscous liquids free from lumps and foreign matter and be non-staining.</p>	Visual inspection on samples weighing about 5 g, drawn from five individual containers from each lot
pH	5.0 to 7.0	Inspection of a composite sample weighing about 10 g, drawn from five individual containers
Viscosity	Shall be within tolerance of ± 1 % of the specified viscosity value	<p>The manufacturer's method of giving equipment, temperature condition, spindle, speed, etc., shall be used.</p> <p>Testing is to be completed on a representative sample from each lot, either from the bulk immediately before packaging or from sufficient individual containers in order to provide an adequate sample size for the viscometer.</p>
Bioburden	<p>Bioburden levels shall be maintained below 100 cfu per gram. There shall be an absence of <i>Pseudomonas aeruginosa</i>, <i>Staphylococcus aureus</i>, <i>Candida albicans</i> and <i>Escherichia coli</i>.</p> <p>Sterility (if claimed) shall be to the sterility assurance level of 10⁻⁶.</p>	<p>Testing as: per <i>The International Pharmacopoeia</i> (14), United States Pharmacopoeia (USP) (15) or European Pharmacopoeia (16).</p> <p>Recommended testing frequency:</p> <ul style="list-style-type: none"> • for the first 10 production lots, every lot shall be tested; • subject to all 10 lots conforming to specification, the testing frequency may be reduced to one in every 10 lots. If a lot fails, then full testing shall be reinstated until 10 consecutive lots have passed.

Table continued

Parameter	Requirements	Verification
Packaging and labelling	Shall comply with requirements of packaging and labelling as given in Section 2, except for material of construction.	Visual observation on samples of 13 containers per lot/batch

References

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