WHO/UNITED NATIONS POPULATION FUND (UNFPA)

SPECIFICATIONS FOR PLAIN LUBRICANTS

(July 2019)

DRAFT FOR COMMENTS

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http://www.who.int/medicines/areas/quality_safety/quality_assurance/guidelines/en

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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 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 the 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, and international organizations that procure lubricants for governments or local organizations.

The status of the WHO/UNFPA/FHI360 Advisory Note on the use and procurement of additional lubricants for male and female condoms published in 2012 (WHO/RHR/12.33) was also reviewed at the Global Consultation. It was agreed that the majority of the recommendations made in that note are still valid and are 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. DESIGN REQUIREMENTS

These shall be verified by review of product dossier.

<table>
<thead>
<tr>
<th>Requirements</th>
<th>Description:</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1. General Requirements</strong></td>
<td>Water-based lubricants shall be clear, translucent or white gels or viscous liquids. They shall be free from lumps and foreign matter, be non-staining and water washable. Silicone lubricants shall be clear, translucent or white gels or viscous liquids free from lumps and foreign matter, and be non-staining.</td>
</tr>
<tr>
<td><strong>Ingredients:</strong></td>
<td>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, non-toxic and shall not liberate any toxic or harmful substance during storage and use.</td>
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<tr>
<td></td>
<td>Lubricants shall be free from added fragrance, colour, spermicides, herbal ingredients and special ingredients which claim specific pleasure enhancing properties.</td>
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<tr>
<td></td>
<td>Silicone lubricants shall contain a minimum of 30% polydimethylsiloxane (dimethicone) with a viscosity of 5 cps and above (mixtures of polydimethylsiloxanes with different viscosities are permitted).</td>
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<tr>
<td></td>
<td><strong>Compatibility with condoms:</strong> Lubricant shall be compatible with male and female condoms (any exceptions shall be noted in the labelling). Testing shall be conducted according to ASTM D7661, ISO 19671:2018 Additional lubricants for male natural rubber latex condoms - Effect on condom strength or equivalent. 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.</td>
</tr>
</tbody>
</table>
**Preservatives:**  
Water-based lubricants shall be preserved against microbial contamination and shall contain suitable preservatives. The lubricant shall be manufactured under suitable condoms to maintain control of bioburden.

**Sterility:**  
Lubricants may be supplied sterile in unit dose containers.

**Manufacturer:**  
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. Lubricant shall have regulatory approval such as CE Mark or US FDA 510(k).

**Lubricity:**  
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 time of use should submit details of the test method and requirement.

### 2. Composition

The manufacturer shall submit to procurement agencies full composition details of lubricant with 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.

Water-based lubricants shall be formulated to comply with following requirements:

a) Osmolality shall be less than 1200 mOsm/kg\(^9\).  
   This osmolality limit can be achieved by keeping the total glycol content below about 8.3 mass fraction (%w/w)\(^10\).

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\(^9\) This requirement is under review and might be revised at a future date  
\(^10\) This limit may be varied depending on the specific glycols used.
b) pH shall be in the range 5.0 to 7.0<sup>11</sup>

c) Viscosity shall be within the tolerance of ± 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.

The manufacturer shall submit to the procurement agency full composition details of the lubricant with 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.

Silicon-based lubricants shall be formulated to comply with the following requirements:

a) Viscosity shall be within a tolerance of ± 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.

b) Lubricants shall contain a minimum of 30% polydimethylsiloxane (dimethicone) with a viscosity of 5 cps and above (mixtures of polydimethylsiloxanes with different viscosities are permitted).

### 3. Biocompatibility

Lubricants shall comply with requirements of biocompatibility assessments conducted in accordance with ISO 10993 – 1, for specific parameters of cytotoxicity (ISO 10993-5) and skin irritation and sensitization (ISO 10993-10)<sup>12</sup>. The toxicity study reports shall be reviewed and interpreted by qualified toxicologist. Full reports of biocompatibility assessments shall be submitted as part of product dossier.

<sup>11</sup>Note: lubricants with a low buffering capacity that do not disturb the pH of the vagina or rectum are preferred.

<sup>12</sup>Note: Some regulatory authorities require acute systemic toxicity to be assessed. For example, the USFDA require acute toxicity testing by intraperitoneal administration.
### 4. Bioburden levels

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 per gram (USP 1111). There shall be an absence of *Pseudomonas aeruginosa, Staphylococcus aureus, Candida albicans* and *Escherichia coli*. These requirements apply to both water-based and silicone-based lubricants.

Bioburden levels shall be maintained at the above levels during storage and repeated opening of container during multiple use.

Lubricants shall comply with the Preservative Efficacy evaluation performed as per the requirements of pharmacopoeia.

If the lubricant is claimed to be sterile, it shall comply with a Sterility Assurance Level of $10^{-6}$.

### 5. Shelf-life and stability

Lubricants shall have a minimum shelf-life of three years from the date of manufacture.

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 %) RH to ensure conformity with Zone IVb requirements.

In line with ICH guideline Q1A(R2), accelerated studies shall be conducted at 40°C ± 2°C/75% RH ± 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.

For water-based lubricants, manufacturers should include freeze thaw cycling in their stability studies to confirm that the lubricants can tolerate freezing.

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.

Lubricants shall remain within the manufacturer’s specification for the duration of the shelf-life period.

The data and report on accelerated stability studies and ongoing real-time studies shall be submitted as part of product dossier.

### 6. Compatibility with condoms

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.

Any exceptions from testing or incompatibilities shall be noted.

### 7. Packaging

**Individual containers:**
Lubricants shall be packed in tamper evident containers facilitating multiple delivery of lubricant. Examples are collapsible/squeeze tubes and containers with a suitable delivery system for application of lubricant.

It is recommended that containers should be made of recyclable materials, compatible with lubricant as substantiated by stability studies and shelf-life claims. The containers shall not have sharp edges. The containers 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.

The recommended nominal contents for multi-dose containers are 35g, 50g and 82g. Other sizes may be considered depending upon programme requirements. The recommended nominal contents for a single dose sachet is 3g for silicone lubricants and 4 to 5g for water-based lubricants.

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.

**Secondary packing:**
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).

Cardboard boxes shall be FSC (or equivalent) marked/certified. They shall only contain paper/cardboard. Plastic coating shall not be used.

**Shipper cartons:**
Shipper cartons shall be FSC (or equivalent) marked/certified. They shall be made of minimum 40% recycled/post-consumer material.

The gross box should only contain paper/cardboard. Plastic coating shall not be used.

The plastic carton liner shall be made from recycled material/plastic and biodegradable plastic by 2020.

<table>
<thead>
<tr>
<th>8. Labelling</th>
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<tbody>
<tr>
<td><strong>Individual containers:</strong> Labelling requirements may be subject to local regulatory requirements. Subject to any local requirements, the individual containers shall be marked with the following details:</td>
</tr>
<tr>
<td>a) Contents (specify if it is water- or silicone-based lubricant).</td>
</tr>
<tr>
<td>b) The quantity of lubricant that can be expressed from the container in normal use.</td>
</tr>
<tr>
<td>c) If in a multi-dose container, advice on the amount of lubricant to be used.</td>
</tr>
<tr>
<td>d) Manufacturer’s name and address.</td>
</tr>
<tr>
<td>e) Batch/lot number.</td>
</tr>
<tr>
<td>f) Expiry date (in YYYY-MM format).</td>
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<tr>
<td>g) Storage conditions – store at an average temperature below 30 °C and avoid exposure to direct sunlight.</td>
</tr>
<tr>
<td>h) Warnings/special notes, if any.</td>
</tr>
<tr>
<td>i) Maximum time period in which the contents can be used after the container was first opened.</td>
</tr>
<tr>
<td>j) A list of any ingredients that may be an irritant or which could cause allergic reactions.</td>
</tr>
<tr>
<td>k) 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).</td>
</tr>
<tr>
<td>l) A statement that lubricant is not a contraceptive and does not protect against pregnancy, sexually transmitted infections and HIV. The lubricant must be used with a condom to protect against pregnancy and sexually transmitted infections.</td>
</tr>
</tbody>
</table>

**Secondary packaging:**

a) Contents.

b) Quantity.

c) Manufacturer’s name and address.

d) Batch/lot number.

e) Manufacturing date and expiry date (in YYYY-MM format).

f) Storage conditions.

g) Warnings/special notes, if any.

Shipper cartons (or as per UNFPA Shipping instructions to be provided by the buyer):

a) UNFPA logo.

b) UNFPA project number.

c) UNFPA purchase order (PO) number.
d) Country of destination.
e) Contents as water-based lubricants.
f) Quantity.
g) Manufacturer’s name and address.
h) Batch/lot number.
i) Manufacturing date (in YYYY-MM format).
j) Expiry date (in YYYY-MM format).
k) Weight.
l) Volume.
m) 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”.
n) Warnings/special notes, if any, to be defined by the manufacturer.
o) Any special shipping instructions defined by the manufacturer.

2.1 Lot by lot testing requirements

The manufacturer shall submit a Certificates 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.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Requirements</th>
<th>Verification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Description</td>
<td>Water-based lubricant shall be clear, translucent or white gel or viscous liquid, free from lumps and foreign matter, non-staining and water washable.</td>
<td>Visual inspection on samples weighing about 5g, drawn from five individual containers from each lot.</td>
</tr>
</tbody>
</table>
Silicone lubricants shall be clear, translucent or white gels or viscous liquids free from lumps and foreign matter and be non-staining.

<table>
<thead>
<tr>
<th><strong>pH</strong></th>
<th>5.0 to 7.0</th>
<th>Inspection on composite sample weighing about 10g, drawn from five individual containers.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Viscosity</strong></td>
<td>Shall be within tolerance of ±10% of the specified viscosity value</td>
<td>The manufacturer’s method of giving equipment, temperature condition, spindle, speed, etc., shall be used. 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.</td>
</tr>
<tr>
<td><strong>Bioburden</strong></td>
<td>Bioburden levels shall be maintained below 100 CFU per gram. There shall be an absence of <em>Pseudomonas aeruginosa, Staphylococcus aureus, Candida albicans and Escherichia coli</em>. Sterility (if claimed) shall be to the Sterility Assurance level of $10^{-6}$</td>
<td>Testing as: per The International Pharmacopoeia (Ph. Int..), U S Pharmacopeia (USP) or European Pharmacopoeia (Ph. Eur.). Recommended testing frequency: 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.</td>
</tr>
<tr>
<td><strong>Packaging and labelling</strong></td>
<td>Shall comply with requirements of packaging and labelling as given in section I, except for material of construction. Labelling languages: English, French, Spanish.</td>
<td>Visual observation on samples of 13 containers per lot/batch.</td>
</tr>
</tbody>
</table>