World Health Organization

REPORTABLE CHANGES TO A WHO PREQUALIFIED MALE CIRCUMCISION DEVICE

WHO PREQUALIFICATION TEAM: DIAGNOSTICS

WHO/MVP/EMP/RHT/PQT/2019.04

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CONTENTS

1. PURPOSE OF THIS DOCUMENT 4
   - 1.1 Intended audience 4
   - 1.2 Scope 4
   - 1.3 Background 4
2. REPORTING OF CHANGES TO WHO 5
3. CHANGES REQUIRING A NEW PREQUALIFICATION APPLICATION 6
4. REPORTABLE CHANGES 6
   - 4.1 Reportable changes to the manufacturing process 7
   - 4.2 Reportable changes to the product 8
   - 4.3 Regulatory status and other changes 9
5. REPORTABLE ADMINISTRATIVE CHANGES 10
6. NON-REPORTABLE CHANGES 10
7. DETERMINING THE IMPACT OF A CHANGE 11
8. REPORTING TO WHO 11
9. ASSESSMENT OF SUBMITTED PQMC CHANGE REPORTING FORMS 12
   - 9.1 Initial screening of reporting form 12
   - 9.2 Review of reporting form 12
   - 9.3 Technical review 12
10. OUTCOME OF ASSESSMENT OF THE CHANGE 13
11. FAILURE TO REPORT A REPORTABLE CHANGE TO WHO 13
12. MONITORING OF CHANGE REPORTING 13
13. CHANGE ASSESSMENT FEE 14
14. RELEVANT DOCUMENTS 15
15. CONTACT INFORMATION 16

ANNEX 1: CHANGE PROCESS 17
ANNEX 2: EXAMPLES OF REPORTABLE CHANGES TO PREQUALIFIED MALE CIRCUMCISION DEVICES 19
ANNEX 3: EXAMPLES OF NON-REPORTABLE CHANGES 22
ANNEX 4: FORMATTING REQUIREMENTS FOR SUBMISSIONS 23
REFERENCES 24

1 PURPOSE OF THIS DOCUMENT

1.1 INTENTED AUDIENCE

This document aims to provide manufacturers of WHO prequalified male circumcision devices with information on when they must report to WHO about:

- changes to the prequalified device or its manufacture;
- changes to the Quality Management System (QMS) that the device is designed and manufactured under; and/or
- other reportable administrative changes.

Manufacturers of WHO prequalified male circumcision devices should read and understand this document so that they are aware of their duties and responsibilities as a supplier of a prequalified male circumcision device as to when to report to WHO applicable changes to the device, its manufacture and other related activities.

Note: for the purpose of this document the following definition of "manufacturer" applies: any natural or legal person with responsibility for design and/or manufacture of a male circumcision device with the intention of making the device available for use, under his/her name; whether or not such a device is designed and/or manufactured by that person himself/herself or on his/her behalf by another person(s) [1].

This document does not address the required response to changes made during the prequalification assessment. For changes implemented during the assessment process, manufacturers should contact WHO to seek guidance.

1.2 SCOPE

This document describes when and how a manufacturer will report to WHO changes to a prequalified male circumcision device and its manufacture, the QMS under which it is manufactured, and certain administrative changes associated with the device. To assist the understanding of when to report a change to WHO, this document provides guidance and a non-exhaustive list of generic examples.

1.3 BACKGROUND

As part of the life cycle of a medical device, changes to the product, and/or its intended use, its manufacturing process or location or the QMS under which it is produced may become necessary for technical or economic reasons. Such changes to a prequalified male circumcision device range from minor, which have little potential to impact the quality, safety, performance or intended use of the device, to substantial, which are likely to affect the quality, safety, performance or intended use of the device. A critical part of a manufacturer's QMS is a documented, controlled and approved process to design, review, verify, validate (if appropriate), approve

and implement changes. As part of this change process, a manufacturer should also determine the significance of the change, on the quality, function, performance, usability, safety, intended use, and applicable WHO requirements for the prequalified male circumcision device and its intended use. Manufacturers should also evaluate the effect of the change on constituent parts of the of the device, on devices that are in-process or have been delivered, and if the change has introduced new hazards that will alter the initial risk analysis and risk control measures. Changes applied to a male circumcision device must be made in conformance with the requirements for control of design change according to ISO 13485:2016 **[2].**

Annex 1 gives an overview of the Change Reporting process and associated sub-processes.

2 REPORTING OF CHANGES TO WHO

For the purpose of this guidance, changes are defined either as **reportable** or **non-reportable.**

All substantial changes and certain administrative changes (information that has an impact on the WHO public report) associated with a prequalified male circumcision device are considered as **reportable changes.** These types of changes must be reported to the WHO Prequalification Team – Diagnostics Assessment at diagnostics@who.int by way of the *"Change Reporting Form for a WHO Prequalified Male Circumcision Device"* (WHO document PQMC_119) and in some cases by way of a new prequalification application.

Unless specified in this document, minor changes associated with a prequalified male circumcision device are considered as **non-reportable** and do not require the submission of a *Change Reporting Form for a WHO Prequalified Male Circumcision Device to WHO.* These types of changes and the manufacturer's justification for not reporting the change are to be documented and controlled in the manufacturer's quality management system.

A **substantial change** is one that is demonstrated, through risk analysis, to have a potential impact on the quality, function, performance, usability, intended use or safety of a prequalified male circumcision device.

It may:

- introduce new hazards that have not been previously addressed;
- adversely affect risks associated with existing hazards; and/or
- alter the presentation of existing or new risks to the user (this can involve labelling changes or new intended uses).

Manufacturers should contact WHO early in the process of designing and validating a change, to allow sufficient time for assessment before the change is implemented.

[a] Some regulatory authorities refer to changes as "variations".
[b] A substantial change is a change that could affect the quality, function, performance, usability, intended use or safety of the prequalified male circumcision device.

3 CHANGES REQUIRING A NEW PREQUALIFICATION APPLICATION

In some cases, changes affect the safety, performance and/or intended use of the device to such an extent that a new application for WHO prequalification assessment is required. This will occur where it is deemed that the changes have resulted in a product, or application information, that is substantially different to that which was prequalified. In these cases, WHO will notify the manufacturer that a new application to WHO prequalification is required. This new prequalification application will undergo prequalification assessment, according to WHO guidance "Overview of the Prequalification of Male Circumcision Devices Assessment Process" (WHO document PQMC_007). WHO will also notify the manufacturer whether there is an impact on the prequalification status of the product as a result of the planned change.

The changes listed below are examples which could require submission of a new application for prequalification:

- a change in design that influences the mode of operation of the device, which would require additional clinical data to comply with the Essential Principles of safety and performance of medical devices **(4)**;
- changes in packaging affecting the sterile barrier system or changes in sterilization process;
- a change to the legal manufacturer that involves the implementation of a different Quality Management System.
- a change that affects the continued compliance of the QMS with the relevant standards.

The combination of several changes can also result in the need for a new prequalification application. Manufacturers should seek advice from WHO when planning to introduce several changes at the same time following the procedure described in Section 8 below.

4 REPORTABLE CHANGES

The following sections provide more details on types of changes that require submission through PQMC *"Change Reporting Form Report Form for a WHO Prequalified Male Circumcision Device"* (WHO document PQMC_119). For a comprehensive list of documentation to accompany the PQMC Change Reporting Form, please refer to Section 4 of the form.

For the purposes of prequalification, reportable changes to a prequalified product are divided into the following categories:

4.1 Changes to the manufacturing process;
4.2 Changes to the product
  4.2.1 Design changes and changes to the intended use;
  4.2.2 Changes to labelling;
4.3 Regulatory status and other changes; and
5. Administrative changes.

4.1 REPORTABLE CHANGES TO THE MANUFACTURING PROCESS

A change to the manufacturing process, facility or equipment that could affect the quality, safety and/or performance of the prequalified male circumcision device is considered a substantial change and thus reportable, therefore requiring the submission of a completed *PQMC Change Reporting Form to WHO.*

Examples of reportable changes to a manufacturing process
Physical move/relocation of finished product manufacturing, assembling or other processing equipment from one location to a different location or; addition of a new facility (manufacturing facility, warehouse, etc.) within the same location.
Change in the manufacturing process such as the introduction of new equipment or change in workflow.
Changes to the manufacturing quality control procedures, such as the methods, tests or procedures used to control the quality of the materials or the product.
Change to the sterilisation method and/or associated processes.
Removal of test acceptance criteria for in-process and finished product. Removal of in-process inspections or final inspections without replacement of these activities.
Addition of in-process inspection steps in response to post-market product issues.
Change of a supplier, or sub-tier supplier, of materials used in the fabrication of the male circumcision device.
Move of manufacturing, processing or packaging from a supplier to the manufacturer's facility.
Move of manufacturing, processing or packaging from the manufacturer's facility to a supplier.

4.2 REPORTABLE CHANGES TO THE PRODUCT

4.2.1 DESIGN CHANGES AND CHANGES TO THE INTENDED USE

Changes to a product may span from minor changes to the design of the product to substantial changes in intended use. All changes must be evaluated, verified and validated according to the accepted procedures recorded in the QMS documentation. Changes to the design specifications, physical attributes, or instructions for use may be substantial if they potentially have an impact on the intended use of the male circumcision device. Additionally, changes to claims relating to the intended use must be reported, even if they do not have an impact on design.

Examples of reportable changes to the product design and intended use
A change to the target population or new indications for use, e.g. an expansion to the age range of males to be circumcised.
A change to (or addition or removal of) a contraindication for use of the device.
A change to the approved requirements and/or method for device use (e.g. change to training requirements, removal of requirements for client access to surgical facilities) which requires preclinical or clinical data to support the continuing safety and performance of the device.
A change to the materials or material formulation, including changes to the device surface or coating, involving materials that contact body tissues or may be absorbed by the body. This includes addition of a colouring agent.
A change to materials/components that necessitate testing to determine performance characteristics of the device, e.g. biocompatibility, tensile strength.
A change to the operating principles not related to a new mechanism of action for the device.
A change to the mode of operation or procedure for application or removal of the device.
A change in performance or design specifications.
A change to (or addition or removal of) a warning or limitation for use of the device.
New data relating to stability impacting on the expiry date, transport or storage conditions of the device.
Changes or deletions to the accessories supplied with the device (e.g. measuring devices, removal accessories, bandages, etc.), if affecting performance and safety of the device;

4.2.2 CHANGES TO LABELLING

For the purposes of WHO Prequalification, labelling includes labels and instructions for use. All changes to labelling should be reported.

Reportable changes to labelling
The following changes will not elicit an assessment/change fee. These changes should be reported to ensure that the WHO Public Reports contains the most current version of the labelling: • Clarify an existing labelling statement (e.g. or safety specificationrewording in IFU without changing the meaning/ instructions procedure; • Correct errors (e.g. typographical errors or numerical errors that do not change the interpreztation of the procedure or safety specification); • Include additional languages; • Change the format of the labels and/or Instructions For Use without removal/addition of content or changing the presentation of risks to the user (e.g. to align with the requirements of international regulatory authorities); and/or • Replacing (or complementing) written text by internationally recognized symbols.

4.3 REGULATORY STATUS AND OTHER CHANGES

Changes to the regulatory status
Change in the regulatory status of the prequalified male circumcision device in any of the member nations or regions of the International Medical Device Regulators Forum (IMDRF) (e.g. licence suspension in Canada, receipt of a Warning Letter from the US FDA, suspension from the Australian Register of Therapeutic Goods, or suspension of a CE mark certification in the European Union).
Change to the classification of the device, such as up-classification by a regulatory authority.
Examples of changes to the QMS
Changes in the ISO 13485 certification status of the manufacturer of the prequalified male circumcision device, such as suspension of the ISO 13485 certificate, obtaining a new certification, or change in the scope of certification.
Change in Notified Body or certification body.
Changes to the legal manufacturer including: • change of ownership; • change of legal entity status (e.g. Ltd, SA, etc.); and • change of name and/or address.

5 REPORTABLE ADMINISTRATIVE CHANGES

Changes limited to the product name, product code(s) and/or manufacturer name require reporting.

Reportable administrative changes
Changes only to the product name.
Changes only to the product code(s).
Changes only to the manufacturer name.

For administrative changes, the following information should be provided with the *PQMC Change Reporting Form:*

- a declaration that the change only affects the product name, product code(s) and/or manufacturer name and has no impact on the quality, safety, performance or intended use, as supported in the submitted prequalification documentation and the reason(s) for making the changes; and
- the new product labelling (labels, instructions for use, and any other printed or electronic labelling material) reflecting the changes.

Changes to the WHO key authorized contact for the manufacturer do not require submission of a PQMC Change Reporting Form but WHO should be notified by email to diagnostics@who.int accompanied by a signed letter from the manufacturer appointing new contacts as authorized to represent the manufacturer for the purposes of prequalification.

6 NON-REPORTABLE CHANGES

All other minor changes that are not required as part of a *PQMC Change Reporting Form* and may include, but are not limited to:

- minor QMS changes such as increased post-market surveillance activity or routine updates of controlled QMS procedures (such as control of documents, management review etc.); not related to any reportable changes as determined by the process in Section 4 above.
- minor manufacturing changes that would not have an effect on the quality, safety or performance of the prequalified male circumcision device;
- deletion or change of a provided accessory (e.g. bandages), if not affecting performance and safety of the device;
- change to packaging design or to a container that is not in direct contact with the device, and which does not have an impact on the integrity of the device during storage or transportation (not applicable if the packaging is sterilized); and/or
- additional in-process quality control criteria or test methods for manufacturing processes to provide equivalent or better assurances of reliability, as determined by the manufacturer but which do not affect safety or performance.

7 DETERMINING THE IMPACT OF A CHANGE

The requirement to report to WHO regarding a change depends on the impact of the change on the quality, safety and/or performance of the male circumcision device. The impact of a change should be determined for all changes. The change to the overall residual risk evaluation for the device may have arisen from:

- actions including field safety corrective actions (e.g. recalls or changes to labelling) taken related to concerns arising from post-market surveillance of complaints and adverse events;
- redevelopment including state of the art product improvements;
- changes to a manufacturing process, facility or equipment;
- changes to the design, components and/or accessories of the prequalified male circumcision device;
- changes to the organization of the manufacturer;
- changes to the intended use and/or instructions for use;
- changes necessitating new pre-clinical and/or clinical data that raise new issues of safety and performance; and/or
- published or unpublished literature raising new issues of safety and performance with the device and/or procedure.

Consideration should be given to the impact of the change on the overall residual risk/benefit evaluation of the male circumcision device as per ISO 14971 **[3].** This includes a determination of whether or not the change:

- introduces new hazards that have not been previously addressed;
- adversely affects the risk associated with existing hazards;
- alters the details of any of the information submitted for prequalification (related to dossier, manufacturing site(s) inspection, technical or clinical evaluation), such as the intended use and/or compliance with the Essential Principles of safety and performance of medical devices **[4];** and/or
- affects the continued compliance of the QMS with the relevant standards.

Where the change is considered substantial, as assessed through the above process, it should be reported to WHO. The steps in the risk analysis rationale used for determining whether a change is reportable or not must be documented.

8 REPORTING TO WHO

The manufacturer should inform WHO of the intention to report a change by email to diagnostics@who.int and subsequently, complete and submit a *PQMC Change Report Form* via **file transfer.** For a comprehensive list of documentation to accompany the *PQMC Change Report Form*, please refer to Section 4 of the form. Formatting requirements are outlined in Annex 4 of this document.

Manufacturers should communicate their intent to introduce a substantial change in advance to allow sufficient time for assessing the change prior to its implementation. WHO will not approve any changes without due assessment. Depending on the type of change, the assessment may also include a manufacturing site(s) inspection.

9 ASSESSMENT OF SUBMITTED PQMC CHANGE REPORT FORMS

9.1 INITIAL SCREENING OF CHANGE REPORTING FORM AND SUPPORTING DOCUMENTATION

Once WHO receives the PQMC Change Reporting Form, the change request will be reviewed to determine the actions required to assess the change.

The report form and documentation (including project plan if appropriate) will be screened for completeness. This screening does not take into consideration the technical appropriateness of all the information provided within the change report. If the provided documentation is incomplete, the manufacturer will be informed and requested to provide supplements within a specified time period set by WHO. The manufacturer will be given one opportunity to provide additional information prior to commencement of the change documentation.

9.2 REVIEW OF CHANGE REPORT FORM AND SUPPORTING DOCUMENTATION

Depending on the type of proposed change, change requests could undergo an "Administrative Review" and/or a "Technical Review".

9.3 TECHNICAL REVIEWS

A Technical Review is performed if the proposed change is not considered "Administrative". Technical reviews are performed if (i) the change is likely to affect the intended use, quality, safety and/or performance of the male circumcision device; or (ii) the change introduces new hazards that have not been previously addressed, could adversely affect risks associated with existing hazards, or could alter the presentation of existing or new risks to the patient or user of the device.

Technical reviews are performed according to WHO document "Overview of the prequalification of male circumcision devices assessment process" (document PQMC_007) and "Framework for Clinical Evaluation of Devices for Male Circumcision". Manufacturers are given one opportunity to address any deficiencies in the submitted documentation and/or findings that may have arisen during the technical review.

If the submitted documentation supporting the change does not meet WHO prequalification requirements or the requested information is not provided by the manufacturer within the specified time period, WHO will reject the change.

10 OUTCOME OF ASSESSMENT OF THE CHANGE

WHO will inform the manufacturer of the outcome of the WHO assessment of the change in writing. The manufacturer will be notified if WHO deems that a manufacturing site inspection and/or a clinical evaluation is required. The need to perform a manufacturing site(s) inspection and/or a clinical evaluation will be established based on the nature of the change and its potential impact on the quality, safety and/or performance.

Where a change is accepted by WHO, the manufacturer may implement the proposed changes to the prequalified male circumcision device. As needed, WHO may update the WHO prequalification public report and its list of prequalified male circumcision devices to reflect the respective change.

If the submitted documentation supporting the change does not meet WHO prequalification requirements or the requested information is not provided by the manufacturer within the specified time period, WHO will reject the change. The impact of such a decision on the prequalification status of the prequalified device will be communicated to the manufacturer.

11 FAILURE TO REPORT A REPORTABLE CHANGE TO WHO

Reporting of changes that meet the criteria for reportable changes, as described in this guidance document, is mandatory for all prequalified male circumcision devices. It is the manufacturer's responsibility to notify WHO of changes, as described in this guidance document, in order to keep the prequalification status of the product up to date. Failure to report changes in accordance with the requirements set in this document may result in the delisting of the product from the list of prequalified male circumcision devices.

12 MONITORING OF CHANGE REPORTING

As part of routine post-prequalification activities, WHO re-inspections will include a review of the compliance of the manufacturer to the requirements of this document. Failure to comply may result in the assignment of a nonconformity against the manufacturer's QMS.

13

CHANGE ASSESSMENT FEE

WHO will review the *PQMC Change Report Form* to determine the type and level of assessment required. The cost of the activities required to assess the change will be covered in part by the manufacturer. WHO charges a non-refundable "Change Assessment Fee" for Technical and Abbreviated Reviews. The fee must be paid on request by WHO and the review will not begin until the payment has been verified. This fee will contribute to the costs associated with change documentation review, manufacturing site(s) inspection, and dissemination of change information.

WHO does not charge a "Change Assessment Fee" for Administrative Reviews.

WHO reserves the right to decide, based on the change assessment findings, whether a product continues to meet prequalification requirements. Payment of the change assessment fee does not guarantee that the change will be approved. WHO also reserves the right to reject the proposed change(s) at any stage if the manufacturer is not able to, or fails to, provide the required information in a specified time period, or when the information supplied is inadequate to complete the change assessment effectively.

[c] Details on the change assessment fee are provided in WHO document PQMC_299 *Prequalification Fees for male circumcision devices.*

14

RELEVANT DOCUMENTS

- WHO Prequalification – Diagnostic Assessment: Overview of the Prequalification of Male Circumcision Devices Assessment Process. WHO PQMC_007, v1, 16 December 2011. Geneva: World Health Organization; 2011.
- ISO 13485:2003 and 2016. Medical devices – Quality management systems – Requirements for regulatory purposes. Geneva: International Organization for Standardization; 2003, 2016.
- ISO 14971:2007. Medical devices – Application of risk management to medical IVDs. Geneva: International Organization for Standardization; 2007.
- IMDRF GRRP WG/N47 FINAL: 2018 Essential Principles of Safety and Performance of Medical Devices and IVD Medical Devices. Medical Device Regulators Forum (IMDRF); 2018.
- FDA: Deciding When to Submit a 510(k) for a Change to an Existing Device (K97-1). Center for Devices and Radiological Health, FDA. Deciding When to Submit a 510(k) for a Change to an Existing Device (K97-1) and Center for Biologics Evaluation and Research (CBER), Silver Spring, MD: Food and Drug Administration; 1997.
- Guidance for Industry and Food and Drug Administration Staff. 30 Day Notices, 135 Day Premarket Approval (PMA) Supplements and 75 Day Humanitarian Device Exemption (HDE) Supplements for Manufacturing Method or Process Change. Center for Devices and Radiological Health (CDRH) and Center for Biologics Evaluation and Research (CBER), MD, USA; 2011.
- Guidance for Industry and Food and Drug Administration Staff. Modifications to Devices Subject to Premarket Approval (PMA) – The PMA Supplement Decision. Center for Devices and Radiological Health (CDRH) and Center for Biologics Evaluation and Research (CBER), MD, USA; 2008.
- Guidance for Industry and Food and Drug Administration Staff. Manufacturing Site Change Supplements: Content and Submission. Center for Devices and Radiological Health (CDRH) and Center for Biologics Evaluation and Research (CBER), MD, USA; 2015.
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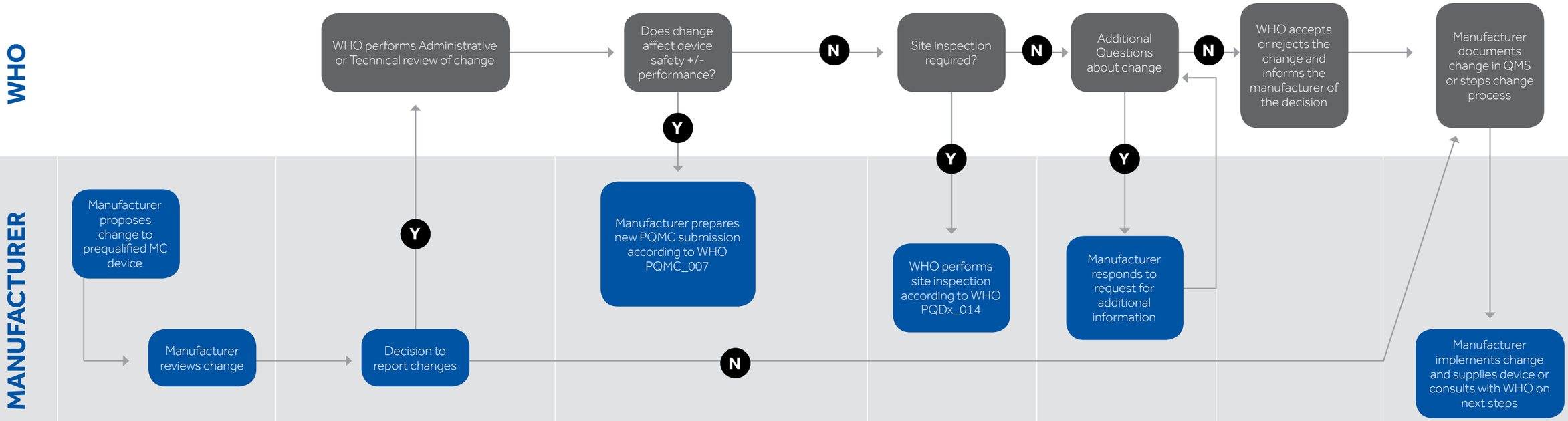
- Real-Time Premarket Approval Application (PMA) Supplements. Center for Devices and Radiological Health (CDRH) and Center for Biologics Evaluation and Research (CBER), MD, USA; 2006.
- NBOG BPG 2014-3 Guidance for manufacturers and Notified Bodies on reporting of Design Changes and Changes of the Quality System. Notified Body Operations Group (NBOG), Bonn, Germany; 2014.
- Health Sciences Authority of Singapore. Medical device Guidance GN-21: Guidance on change notification for registered medical devices. Revision 4. Singapore; 2015.
- Changes or variations to therapeutic devices in the ARTG. Therapeutic Goods Administration (TGA). ACT, Australia; 1998.
- Health Canada: Guidance for the Interpretation of Significant Change of a Medical Device. Health Products and Food Branch, Ottawa, Ontario; 2011.
- WHO HIV/AIDS Programme: Framework for clinical evaluation of devices for male circumcision. Geneva: World Health Organization; 2012.

15 CONTACT INFORMATION

Any inquiries regarding changes to prequalified male circumcision devices should be addressed to: diagnostics@who.int

ANNEX 1: CHANGE PROCESS



DESCRIPTION

Manufacturer determines information needed to assess impact of the change.

Manufacturer determines impact of the change on the prequalified device.

Manufacturer retains:

Result of risk analysis.

Review of risk assessment.

Manufacturer categorizes change as substantial (reportable) or minor (non-reportable).

Manufacturer documents the answers to the following questions.

1) Is the change a simple administrative change to just the product name, product code(s), or the manufacturer's name?

2) Does the change:

- Introduce new hazards that have not been previously addressed?
- Adversely affect risks associated with existing hazards? and/or
- Alter the presentation of existing or new risks to the user?

If the manufacturer answers No to all of the questions above then the change is non-reportable and manufacturer is required to document and control the change according to its QMS procedures.

If the manufacturer answers Yes to any of the questions above, then the change is reportable, and the Manufacturer is required to submit via courier an electronic copy of a completed PQMC Change Form (WHO document PQMC_119) and any supporting information via file transfer.

For reportable Administrative changes WHO does not charge a change assessment fee.

For reportable changes that require a Technical Review, WHO charges a non-refundable change assessment fee of USD $3,000 that must be paid before WHO will begin a review.

If the change affects the safety and/or performance of the device, as per section 3, then the Manufacturer must submit a new "Prequalification Application" (document WHO PQMC_015) to WHO for review. WHO's review process follows WHO guidance document PQMC_007

If WHO considers that the change could have a potential impact on the quality, safety and/or performance of the device, then WHO may perform a site inspection prior to making a final decision to accept the reported change.

Site inspection follows WHO guidance document PQDx_014

Manufacturer answers specific questions about the change and submits them to WHO within the specified time period.

If WHO accepts the change, the manufacturer implements the change then supplies the changed device. WHO updates both the public record and its list of prequalified products and verifies implementation at its next site inspection.

If WHO rejects the change, the manufacturer stops the change process and consults with WHO on next steps.

ANNEX 2: EXAMPLES OF REPORTABLE CHANGES TO PREQUALIFIED MALE CIRCUMCISION DEVICES

The following list is intended as an aid to manufacturers to help determine the significance of particular changes. The list is not exhaustive and should be considered in conjunction with the guidance provided in this document.

TYPES OF REPORTABLE CHANGES
Changes to a manufacturing process
Physical move/relocation of finished product manufacturing, assembling or other processing equipment from one location to a different location or; addition of a new facility (manufacturing facility, warehouse, etc.) within the same location.
Change in the manufacturing process such as the introduction of new equipment or change in workflow.
Changes to the manufacturing quality control procedures, such as the methods, tests or procedures used to control the quality of the materials or the product.
Removal of test acceptance criteria for in-process and finished product. Removal of in-process inspections or final inspections without replacement of these activities.
Addition of in-process inspection steps in response to post-market product issues.
Change of a supplier, or sub-tier supplier, of device materials used in the fabrication of the male circumcision device.
Move of manufacturing, processing or packaging from a supplier to the manufacturer's facility.
Move of manufacturing, processing or packaging from the manufacturer's facility to a supplier.
Change that affects the microbial quality by increasing the bioburden alert or action levels or introducing an organism that is more difficult to kill.
Device design and/or material changes that introduce a feature that makes the device more difficult to sterilize.
Change to the sterilization method and/or associated processes.
Change in the density or configuration of the sterilization load.

Change to the quality control verification and validation process for sterilization such as introducing parametric release.
Change in the packaging of medical devices subject to sterilization.
Changes to the product design and intended use
A change to the target population or new indications for use, e.g. an expansion to the age range of males to be circumcised.
A change to (or addition or removal of) a contraindication for use of the device.
A change to the approved requirements and/or method for device use (e.g. change to training requirements, removal of requirements for client access to surgical facilities) which requires preclinical or clinical data to support the continuing safety and performance of the device.
A change to the materials or material formulation, including changes to the device surface or coating, involving materials that contact body tissues or may be absorbed by the body. This includes addition of a colouring agent.
A change to materials/components that necessitate testing to determine performance characteristics of the device, e.g. biocompatibility, tensile strength.
A change to the operating principles not related to a new mechanism of action for the device.
A change to the mode of operation or procedure for application or removal of the device.
A change in performance or design specifications.
A change to (or addition or removal of) a warning or limitation for use of the device.
New data relating to stability impacting on the expiry date, transport or storage conditions of the device.
Changes or deletions to the accessories supplied with the device (e.g. measuring devices, removal accessories, bandages), if not affecting performance and safety of the device;
Changes in materials/components
Changes to materials/components that necessitate testing to determine performance characteristics of the device, e.g. biocompatibility, tensile strength.

Addition of a colouring agent to materials that are in contact with the patient's body.
Changes to labelling
The following changes will not elicit an assessment/change fee. These changes should be reported to ensure that the WHO Public Reports contains the most current version of the labelling: 1. Clarify an existing labelling statement (e.g. or safety specification rewording in IFU without changing the meaning/instructions procedure; 2. Correct errors (e.g. typographical errors or numerical errors that do not change the interpretation of the procedure or safety specification); 3. Include additional languages; 4. Change the format of the labels and/or Instructions For Use without removal/addition of content or changing the presentation of risks to the user (e.g. to align with the requirements of international regulatory authorities); and/or Replacing (or complementing) written text by internationally recognized symbols.
Changes to the QMS
Changes in the ISO 13485 certification status of the manufacturer of the prequalified male circumcision device, such as suspension of the ISO 13485 certificate, obtaining a new certification, or change in the scope of certification.
Change in Notified Body or certification body.
Changes to the legal manufacturer including: • change of ownership; • change of legal entity status (e.g. Ltd, SA, etc.); and • change of name and/or address.
Change in the regulatory status
Change in the regulatory status of the prequalified male circumcision device in any of the member nations or regions of the International Medical Device Regulators Forum (IMDRF) (e.g. licence suspension in Canada, receipt of a Warning Letter from the US FDA, suspension from the Australian Register of Therapeutic Goods, or suspension of a CE mark certification in the European Union).
Change to the classification of the device by a regulatory authority (e.g. a change in classification from Class III to Class IV).

Administrative changes
Changes only to the product name.
Changes only to the product code(s).
Changes only to the manufacturer name.

ANNEX 3: EXAMPLES OF NON-REPORTABLE CHANGES

The following list is intended as an aid to manufacturers to determine the significance of particular changes. The list is not exhaustive and should be considered in conjunction with the guidance provided in this document.

MINOR CHANGES INCLUDE THE FOLLOWING CHANGES
1. Translating the label and/or IFU from one language to another.
2. Addition of languages to labelling.
3. Replacing (or complementing) written text by internationally recognized hazard symbols.
4. Minor QMS changes such as increased post-market surveillance activity or routine updates of controlled QMS procedures (such as control of documents, management review, etc.) that are not related to any reportable changes as determined by the process in Section 4 above.
5. Minor manufacturing changes that would not have an effect on the quality, safety or performance of the prequalified male circumcision device;
6. Deletion or change of a provided accessory (e.g. bandages), if not affecting performance and safety of the device;
7. Change to packaging design or to a container that is not in direct contact with the device, and which does not impact the integrity of the device during storage or transportation (not applicable if the packaging is sterilized); and/or
8. Additional in-process quality control criteria or test methods for manufacturing processes to provide equivalent or better assurances of reliability, as determined by the manufacturer but which do not affect safety or performance.

ANNEX 4: FORMATTING REQUIREMENTS FOR SUBMISSIONS

- The electronic copy must be submitted via **file transfer.** Hardcopies are not required.
- The layout and order must be easy to follow and appropriately identified. The attachments must be clearly identified and divided into sections as listed in Section 4 of the PQMC Change Report Form.
- The cover of the CD or DVD should indicate "Change Report Form" and include detailed information such as the name of the product, PQMC number, name of the manufacturer and date of submission.
- PDF is the primary file format used for the electronic copy. However, any documents provided in this format must not be password protected.
- The electronic copy must be organized as per the format prescribed for the printed copy.
- The name of the file name should be descriptive of its content and meaningful to the reviewers. The name can be up to 125 characters and can have spaces, dashes (not elongated dashes), underscores, and periods. However, the name of the file must not contain any of the following special characters or it will fail the loading process:

• tilde (~)	• single quotation mark (')
• vertical bar (|)	• less than sign (<)
• asterisk (*)	• double quotation marks (")
• forward slash (/)	• question mark (?)
• elongated dash (–)	• colon (:)
• backward slash (\)	• pound sign (#)
• apostrophe (')	• various other symbols (e.g. → ,β,α,∞,±,™, ®)
• greater than sign (>)	

- When creating a PDF from the source document (e.g. Microsoft Word document), please consider when using Adobe plug-ins to create PDF files and/or capture or display data, there is a risk that information may not display correctly because reviewers may not have access to certain plug-ins to review content being displayed by a plug-in.
- All PDF files should be created directly from the source documents whenever feasible rather than creating them by scanning. PDF documents produced by scanning paper documents are inferior to those produced directly from the source document, such as a Microsoft Word document, and, thus should be avoided if at all possible. Scanned documents,particularly tables and graphs, are more difficult to read.
- For any scanned document, it is highly recommend that an optical character recognition (OCR) is performed so that the text is searchable. A check should also be performed to confirm that content has been correctly converted by: (i) highlighting an area of text and (ii) searching for a word or phrase. If the word or phrase is not returned in the search, then the OCR did not recognize the text.

- Submit all documents presented in the change report in English (unless other arrangements have been made with WHO prior to submission of the documentation).
- Any translations of documents must be carried out by a certified translator and accompanied by an official document attesting to the accuracy of the translation and details on the credentials of the translator.
- Provide both the original and the translated documents.
- All measurement units used must be expressed in the International System of Units (SI).

REFERENCES

1. GHTF/SG1/N071:2012 Definition of the Terms 'Medical Device' and 'In Vitro Diagnostic (IVD) Medical Device'. Global Harmonization Task Force (GHTF) Steering Committee; 2012.

2. ISO 13485:2003 and 2016. Medical devices – Quality management systems – Requirements for regulatory purposes. Geneva, Switzerland: International Organization for Standardization; 2003, 2006.

3. ISO 14971:2007. Medical devices – Application of risk management to medical devices. Geneva: International Organization for Standardization. Geneva, Switzerland; 2007.

4. GHTF/SG1/N68:2012N41R9:2005 Essential Principles of Safety and Performance of Medical Devices. Global Harmonization Task Force (GHTF) Steering Committee; 2012.2005.

List of related WHO Publications of related interest

Change reporting form for a WHO Prequalified Male Circumcision Device, WHO PQMC_119. Geneva, Switzerland: World Health Organization. Available online.

WHO Prequalification Team – Diagnostic Assessment: Instructions for Compilation of a Product Dossier, WHO PQMC_18. Geneva, Switzerland: World Health Organization. Available online.

This document provides guidance and a non-exhaustive list of generic examples, on when and how a manufacturer will report to WHO changes to a prequalified male circumcision device, its manufacture, the quality management system under which it is manufactured and administrative changes.