

WHO Prequalification of Male Circumcision Devices PUBLIC REPORT

Product: PrePex
Number: PQMC 0001-001-04

Abstract

PrePex with product codes **DW0201, DW0202, DW0203, DW0204, DW0205**, manufactured by **Circ MedTech Limited, CE-marked regulatory version**, was accepted for the WHO list of prequalified male circumcision devices and was listed on 31 May 2013. The public report was amended on 2 March 2016 to reflect the expanded intended use on adolescents aged 13 years and above. The public report was amended on 12 July 2016 to reflect a new legal manufacturer; **Circ MedTech Limited, BVI**. The public report was amended on 19 August 2016, to reflect additional sizes with product codes **P6107, P7107, P8107, P9107** manufactured by **Circ MedTech Limited, BVI**. The public report was amended on 9 November 2016, to reflect approval of an additional site of manufacture; Juno Pacific Inc., 1040 Lund Boulevard, Anoka, MN, 55303, USA with additional new product codes for products manufactured at Juno Pacific **AA107, BB107, CC107, DD107** and **EE107**.

Intended use:

PrePex is a single use, disposable device; indicated for circumcision of men aged 13 years and above, defined as circumferential excision of the foreskin or prepuce at or near the level of coronal sulcus, with minimal amount of preputial skin remaining.

The device should not be used if the package has been compromised. Use by trained personnel only. All device components should not be reused at the risk of cross contamination. The device is intended for adult and adolescent males aged 13 years and above. The device should be used only in settings where suitable surgical facilities and skills are available within a short time frame (6-12 hours) in order to manage potentially serious complications resulting from device displacements.

Device displacement when wearing the device, may lead to the risk of adverse events. Informing the patient of safe behavior when wearing the device is critical.

PrePex includes the following items:

1. Placement Ring
2. Elastic Ring
3. Inner Ring
4. Verification Thread

Accessories:

The PrePex Sizing Plate (PSP) is intended for single use for selecting an appropriate device size. The use of PrePex requires additional tools and materials which are not supplied with PrePex.

For Placement: examination gloves, 10% povidone iodine (PI) solution, skin marker, gauze, 5% anesthetic cream and nurse utility scissors. Additional PSP may be required, if more than one is required to select the correct size.

For Removal: examination gloves, 10% povidone iodine (PI) solution, sterile Harvey wire scissors, sterile forceps, sterile spatula, sterile scalpel, and 5 wound dressings.

Storage:

The test kit should be stored at -10 to 55 °C.

Shelf-life:

3 years.

Warnings/limitations:

As per manufacturer's instructions for use.

One of the risks of using PrePex is contracting tetanus. PrePex is used in countries that may not have widespread coverage of tetanus immunization. Therefore, it is imperative to ensure that all PrePex clients are protected by adequate vaccination with tetanus toxoid containing vaccine (TTCV)¹ prior to placement of the PrePex device.

Warning:

- Do not place PrePex on clients that are not adequately immunized against tetanus.
- Follow acceptable medical guidance to ensure clients are immunized against tetanus.
- Failing to ensure proper immunization may put clients at risk of tetanus.

¹ See The immunological basis for immunization series. Module 3 : Tetanus Update 2006.

Summary of prequalification status for PrePex

	Initial acceptance	
	Date	Outcome
PQ amended	9 November 2016 19 August 2016 12 July 2016 2 March 2016	listed
Status on PQ list	31 May 2013	listed
Dossier assessment	08 October 2012	MR
Inspection status	18 August 2015	MR
Clinical study	28 February 2013	MR

MR: Meets Requirements

N/A: Not Applicable

PrePex was accepted for the WHO list of prequalified male circumcision devices on the basis of data submitted and publicly available information.

Background information

Circ MedTech Limited submitted an application for prequalification of PrePex. Based on the established prioritization criteria, PrePex was given priority for prequalification.

Product dossier assessment

The Manufacturer submitted a product dossier for PrePex as per the *Instructions for compilation of a product dossier* (PQMC_018 v1). The information submitted in the product dossier was reviewed by WHO staff and external experts (assessors) appointed by WHO in accordance with the internal report on the screening and assessment of a product dossier (PQMC_009 v1). Based on the product dossier screening and assessment findings, a recommendation was made to accept the product dossier for PrePex for prequalification.

Manufacturing site inspection

A comprehensive inspection was performed at the site of manufacture Circ MedTech Limited, 6 Hahoshlim St., 1st Floor Herzelia, 46722, Israel and 3BY, 24959 Industrial Park, P.O. Box 65, Migdal Tefen, Israel of PrePex in 18-19 January 2012 and a re-inspection of the same two sites was performed in 5-7 November 2012 as per the *Information for manufacturers on prequalification inspection procedures for the sites of manufacture of diagnostics* (PQDx_014 v1). An additional inspection of Juno Pacific (supplier to CircMedTech) was conducted between 6-8 October 2014 at 1100 McKinley Street, Anoka, Minnesota, 55303 and 1040 Lund Boulevard, Anoka, Minnesota, 55303, USA. The

inspections found that the manufacturer had an acceptable quality management system and good manufacturing practices in place that ensured the consistent manufacture of a product of good quality. The manufacturer's responses to the nonconformities found at the time of the inspection were accepted 30 January 2013. A special inspection was conducted on 14 -16 July 2015. The manufacturer's responses to the nonconformities found at the time of the inspection were accepted on 18 August 2015.

Commitments for prequalification:

1. The manufacturer has committed to continuing improvements in the quality management system particularly in the areas of documented procedures to ensure that supplied product conformed to specified purchase requirements, planned controlled conditions to ensure consistent quality of manufactured product particularly at scale up and internal audits to assure the QMS conformed to planned arrangements.
2. The manufacturer has committed to effective communication of accurate information to customers/end users, planned arrangements for verifying that product requirements have been met, compliance with management review requirements and defined operations for labeling and packaging together with ongoing communication over time to finalize any outstanding issues noted in the WHO responses to the inspection findings.

Clinical evidence review

The WHO Technical Advisory Group (TAG) on Innovations in Male Circumcision concluded that the range and scope of clinical studies met the WHO requirements for evaluation of a device; and demonstrated that, for the purposes of HIV prevention, the PrePex device can efficaciously and safely circumcise healthy males 13 years and over, when used by suitably trained providers, and when surgical backup facilities and skills are available to manage device displacements or early removals that could result in serious complications. The TAG advised that: effective training materials are available and PrePex providers are appropriately trained; men receive accurate information on safe device use and risks while wearing a device, and PrePex is used only in settings where suitable surgical facilities and skills are available within a short time frame (6-12 hours). The extension of use to younger ages is based on limited data, and therefore, the age range must be reassessed when more experience and data are generated from active surveillance to further inform safe use.

Studies reviewed:

Ten studies from 4 African countries satisfactorily met the criteria in the WHO Framework for Clinical Evaluation of Devices. Eight studies included only healthy males 18 years and older, and two studies included men aged 13 – 17 years². The device was placed

² The study conducted in South Africa included 89 adolescents, mostly 16–17 years of age. The proportion excluded due to adhesions or phimosis was not reported. Although numbers were small, the AE rates appeared similar in adolescents and older men, but healing time was significantly shorter in the adolescents. Further details and a full report from the study are awaited.

successfully on 2417 eligible men aged 18 years or above and 402 adolescent boys aged 13 – 17 years.

Eligible:

Males 13 years and older; without contraindications to conventional male circumcision surgery, and additionally, without contraindications specific to PrePex: including phimosis, narrow foreskin, tight frenulum, adhesions.

The proportion of clients not eligible for the PrePex procedure due to adhesions or narrow foreskin was considerably higher among younger adolescents than in men aged 18 years or older, specifically: 53% ineligible among 13 year olds, 40% in 14 year olds, 29% in 15 year olds, and 11% in 16-17 year olds. This compares with 5-7% in adults.³

Among males on whom the device was placed, 99.5% had a successful circumcision for men aged 18 years and above, and 99.8% for adolescent boys aged 13-17 years without surgical intervention and a resulting wound line without suture marks.

Requirements for device use:

At least two visits are required; during the interval the client must wear the device.

- Placement: adequate supply of all device sizes plus accessory supplies and two trained providers, surgical skin preparation, local topical (not injectable) anesthesia.
- While wearing the device for 1 week: analgesia as needed, and access within six to twelve hours to conventional surgical skills and facilities to manage device displacements or early removals (including self-removals) and prevent serious long-term sequelae.
- Removal: requires a clean setting and some sterile accessory equipment. Accessory supplies and equipment are not provided by the device manufacturer.

Safety, healing and discomforts:

All AEs observed in studies were reviewed and classified by the TAG in a uniform manner, guided by internationally recognized principles (Global Harmonization Task Force) and definitions of AEs and serious adverse events (SAEs) which differed somewhat from the definitions and classification used by study investigators.

Adverse events occurred among 1.7% of adults aged 18 years or above; the majority were Mild and Moderate, while 0.4% were considered Serious as prompt surgical intervention was required to prevent serious long-term sequelae (in all cases surgical intervention was successful with no complications and satisfactory outcomes). The rate of serious adverse events for adolescent boys aged 13 - 17 years was similar. The AE rate was lower among men who had PrePex circumcision than among men who had conventional surgery, but

³ Please note sizes A – E were used in this study.

this difference was not statistically significant. No mechanical failures were reported. Healing time for adults appears to be about 1 – 2 weeks longer than following conventional surgical circumcision. Some pain occurred with PrePex procedures, primarily during the first few days after placement and briefly on removal of the device. Complaints of unpleasant odour were also noted by some study participants and providers.

Client information must clearly indicate that once placed, the device must remain for seven days; in case a client desires to remove the device, clients must be instructed to return to the clinic and conventional surgery may be required to complete the circumcision. Clients must also be instructed on safe behaviours while the device is worn, including avoidance of sexual activity and masturbation, the risks associated with misuse and possible surgical intervention required. Clients need to be informed of the possibility of displacement, pain and/or odor while wearing the device.

Change notifications

In 2015, Circ MedTech Limited submitted a change notification related to expansion of the intended use of the product to adolescent males. This change notification was assessed and product was found to meet WHO prequalification requirements with the qualification of further review from active surveillance among 13 - 17 year olds in at least three countries.

In 2016, Circ MedTech Limited submitted a change notification related to a change in the legal manufacturer to Circ MedTech Limited, BVI. This change notification was assessed and product was found to meet WHO prequalification requirements.

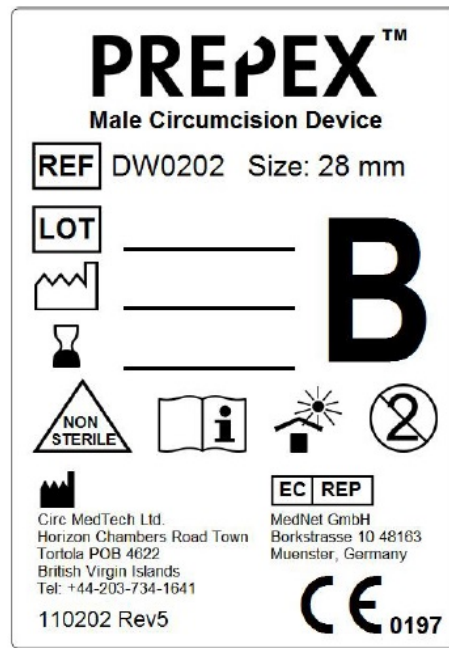
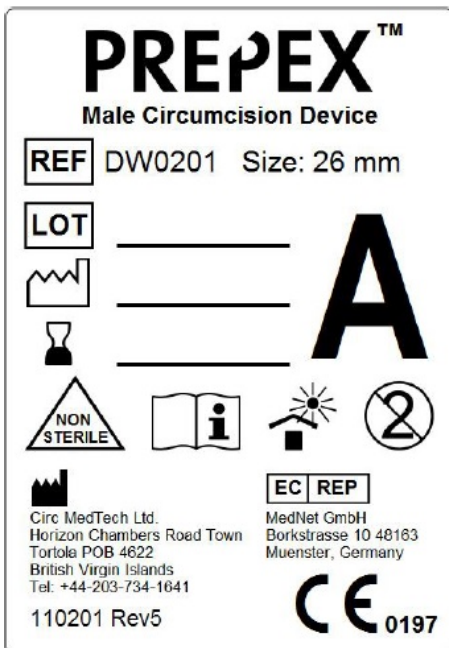
In 2016, Circ MedTech Limited BVI submitted a change notification related to additional device sizes. This change notification was assessed and product was found to meet WHO prequalification requirements.

In 2014, Circ MedTech BVI submitted a change notification related to an additional manufacturing site. This change notification was assessed through documentary review and site inspection and found to meet WHO prequalification requirements.

In 2016, Circ MedTech BVI submitted a request to change the labeling for all products related to warnings for risk of tetanus. This change notification was assessed and product was found to meet WHO prequalification requirements.

Labelling


1. Labels




PREPEX™
Male Circumcision Device





REF DW0203 Size: 30 mm


LOT _____

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 _____

C

 **EC REP**

Circ MedTech Ltd.
Horizon Chambers Road Town
Tortola POB 4622
British Virgin Islands
Tel: +44-203-734-1641


MedNet GmbH
Borkstrasse 10 48163
Muenster, Germany


110203 Rev5 **CE** 0197

PREPEX™
Male Circumcision Device





REF DW0204 Size: 32 mm


LOT _____

 _____

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D

 **EC REP**

Circ MedTech Ltd.
Horizon Chambers Road Town
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Tel: +44-203-734-1641


MedNet GmbH
Borkstrasse 10 48163
Muenster, Germany


110204 Rev5 **CE** 0197

PREPEX™
Male Circumcision Device





REF DW0205 Size: 34 mm


LOT _____

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E

 **EC REP**

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Tortola POB 4622
British Virgin Islands
Tel: +44-203-734-1641


MedNet GmbH
Borkstrasse 10 48163
Muenster, Germany


110205 Rev5 **CE** 0197

PREPEX™
Male Circumcision Device





REF P6107 Size: 18 mm


LOT _____

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P6

 **EC REP**

Circ MedTech Limited
Hanagar 1 Hod Hasharon,
4501305 Israel,
+972506306313

MedNet GmbH
Borkstrasse 10 48163
Muenster, Germany





110306 Rev0 **CE** 0197

PREPEX™
Male Circumcision Device


REF P7107 Size: 20 mm

LOT _____

P7

NON STERILE

 **EC REP**

Circ MedTech Limited
Hanagar 1 Hod Hasharon,
4501305 Israel,
+972506306313

MedNet GmbH
Borkstrasse 10 48163
Muenster, Germany





110307 Rev0 **CE** 0197

PREPEX™
Male Circumcision Device


REF P8107 Size: 22 mm

LOT _____

P8

NON STERILE

 **EC REP**

Circ MedTech Limited
Hanagar 1 Hod Hasharon,
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MedNet GmbH
Borkstrasse 10 48163
Muenster, Germany





110308 Rev0 **CE** 0197

PREPEX™
Male Circumcision Device


REF P9107 Size: 24 mm

LOT _____

P9

NON STERILE

 **EC REP**

Circ MedTech Limited
Hanagar 1 Hod Hasharon,
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+972506306313

MedNet GmbH
Borkstrasse 10 48163
Muenster, Germany

110309 Rev0 **CE** 0197

PREPEX™ CircMedTech public healthcare solutions

LOT _____

NON STERILE

A

Size: 26mm

REF AA107

CE 0197
110206, Rev. 04

Circ MedTech Ltd.
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Tortola POB 4622, British Virgin Islands
Tel: +44-203-734-1641

PREPEX™ CircMedTech public healthcare solutions

LOT _____

NON STERILE

B

Size: 28mm

REF BB107

CE 0197
110207, Rev. 04

Circ MedTech Ltd.
Horizon Chambers Road Town
Tortola POB 4622, British Virgin Islands
Tel: +44-203-734-1641

PREPEX™ CircMedTech public healthcare solutions

LOT _____

NON STERILE

C

Size: 30mm

REF CC107

CE 0197
110208, Rev. 04

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Tortola POB 4622, British Virgin Islands
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PREPEX™ CircMedTech public healthcare solutions

LOT _____

NON STERILE

D

Size: 32mm

REF DD107

CE 0197
110209, Rev. 04

Circ MedTech Ltd.
Horizon Chambers Road Town
Tortola POB 4622, British Virgin Islands
Tel: +44-203-734-1641

PREPEX™ CircMedTech public healthcare solutions

LOT _____

NON STERILE

E

Size: 34mm

REF EE107

CE 0197
110210, Rev. 04

Circ MedTech Ltd.
Horizon Chambers Road Town
Tortola POB 4622, British Virgin Islands
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2. Instructions for use

PREPEX™ by Circ MedTech Ltd.

Instructions for Use: for Authorized & Trained Users

Intended use:

PrePex is a single use, disposable, non-sterile device, indicated for circumcision of men aged 13 and above, defined as circumferential excision of the foreskin or prepuce at or near the level of coronal sulcus, with minimal amount of preputial skin remaining.

Intended Users: Physicians and nurses that have been trained and authorized to perform the PrePex procedure.

Contraindications:

Use of the PrePex device on men who have penis size smaller than size P6 is contraindicated until further notice.

Dermatitis of the penis or foreskin; allergy to rubber; non-intact skin on the penis or foreskin; active genital infection; warts on the glans or the foreskin; anatomic abnormalities, including narrow prepuce, phimosis, paraphimosis, torn or tight frenulum, hypospadias, or epispadias; any active penile diseases; active infectious disease impairing health; history of bleeding disorders; adhesions; any condition that prevents complete retraction of the foreskin and exposure of the entire sulcus.

For all of the above contraindications, patients should be offered surgical circumcision.

Warnings:

Providers must be trained to recognize the following:

- when a patient is not eligible for the PrePex due to inability to retract the foreskin;
- discomfort while attempting to retract the foreskin;
- when there are adhesions or phimosis.

Failure to recognize non-eligibility is likely to lead to adverse events such as increased infection risk due to failure of adequately prepare the skin prior to device placement or incomplete skin removal due to failure to apply the device in the correct anatomical position.

One of the risks of using PrePex is contracting tetanus. PrePex is used in countries that may not have widespread coverage of tetanus immunization. Therefore, it is imperative to ensure that all PrePex clients are protected by adequate vaccination with tetanus toxoid containing vaccine (TTCV)[1] prior to placement of the PrePex device.

Warning:

Do not place PrePex on clients who are not adequately immunized against tetanus.

Follow acceptable medical guidance to ensure clients are immunized against tetanus.

Failing to ensure proper immunization may put clients at risk of tetanus.

1 References

1. Immunological basis for immunization - Module 3: Tetanus (Revision)
<http://www.who.int/immunization/documents/ISBN9789241595551/en/>
2. WHO Weekly epidemiological record 19 MAY 2006, No. 20, 2006, 81, 197-208
http://www.who.int/immunization/wer8120tetanus_May06_position_paper.pdf?ua=1

Disposal:

Follow local, state, and federal regulations with respect to environmental protection when disposing of general and infectious waste. In the absence of regulations, the infectious waste, including all single use device elements, tools, and materials that came in contact with the body or bodily fluids should be incinerated. Other general waste should be segregated and stored in bins marked "General". The waste should then be buried in a designated area.

Caution:

The device must not be used if the package has been compromised. Please verify that the package is intact prior to opening it. Visual inspection of the package edges can identify a compromised package. Use by trained personnel only. All device components must not be reused to prevent risk of cross contamination. The device is intended for men aged 13 and above and is not applicable for males under the age of 13. The device should be used only in settings in which suitable surgical facilities and skills are available within a short time frame (6-12 hours) in order to manage potentially serious complications resulting from device displacements. Device displacement when wearing the device may lead to the risk of adverse events. Informing the patient of safe behavior when wearing the device is critical. Patients must return to the clinic if the device has moved from its original placement location.

Environmental Requirements and Storage Conditions:

Storage: -10 °C to 55 °C, away from direct sunlight.

Shelf Life:

The PrePex expiration date is listed on the label following the manufacturing date.

Device Overview:

PrePex includes the following items:

1. Placement Ring
2. Elastic Ring
3. Inner Ring
4. Verification Thread



Accessories:

The PrePex Sizing Plate (PSP) to select an appropriate device size is intended for single use.

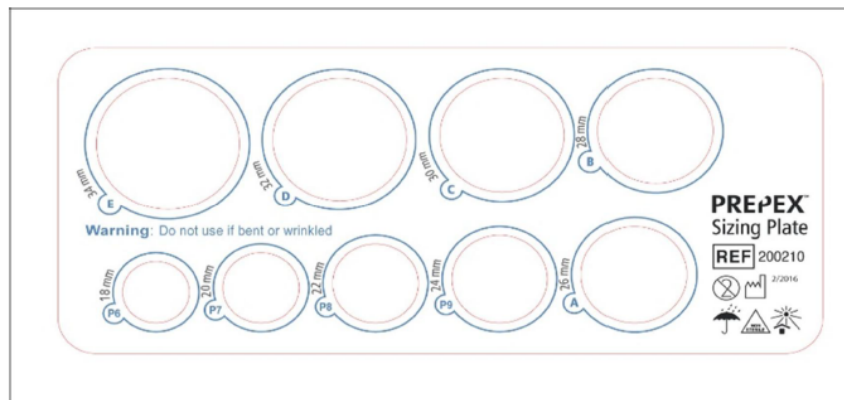


Figure 2 – The PrePex Sizing Plate (PSP)

The use of PrePex requires additional tools and materials that are not supplied with the PrePex device. For placement: examination gloves, 10% povidone iodine (PI)

solution, skin marker, gauze, 5% anesthetic cream and nurse utility scissors. For removal: 10% povidone iodine solution, examination gloves, sterile Harvey wire scissors, sterile forceps, sterile spatula, sterile scalpel, 5 wound dressings. Because after measurement using the PSP some patients will be excluded due to small penis size, there may be an excess of unused devices. Hence it is recommended that extra PSP are purchased to ensure non-wastage of devices.

Patient Screening:

Before performing the procedure, screen the patient for any contraindications and physically test if the opening of the foreskin is wide enough for the PrePex procedure. Perform the test with examination gloves. Stretch the foreskin as described in step 3 of the placement procedure below, and visually assess the flexibility of the foreskin and the opening. If there is narrow opening, phimosis, or tight frenulum or adhesions that prevent complete retraction of the foreskin and complete exposure of the sulcus; the patient is not eligible for PrePex. Gently pull the foreskin down to expose the sulcus and examine whether the foreskin is tight in the area below the sulcus. If the foreskin is tight in the area below the sulcus, the patient is not eligible for PrePex. It is important not to use excessive force when pushing the Inner Ring through the foreskin opening.

Warning: For all of the above contraindications, patients should be offered surgical circumcision.

Patient Preparation and Procedure:

The patient must assure their personal hygiene, including cleaning of the genital area and under the foreskin with soap and water prior to PrePex Placement procedure to remove any dirt and/or debris

For adolescent consent follow local law and regulations.

During the PrePex MC procedure, providers must wear examination gloves after washing hands.

Standard surgical disinfection protocols for skin preparation should be followed prior to PrePex Placement and Removal. Disinfection of the genital region and the penis should be performed after fully retracting the foreskin using appropriate disinfectants. Use of Povidone-iodine (PI) is recommended, unless there is a known allergy. Apply at least 3 applications; waiting at least 2 minutes before proceeding with the procedure. A detailed disinfection procedure is provided below.

1. Use a new, single-use PSP. Select the appropriate size P6, P7, P8, P9, A, B, C, D, or E by sliding each opening of the PSP over the glans and placing it directly under the coronal sulcus. The appropriate size is the opening which fits best (Figure 3).
2. Choose PrePex based on the sizing outcome (P6, P7, P8, P9, A, B, C, D, or E).

Type	Diameter
P6	18mm
P7	20mm
P8	22mm
P9	24mm
A	26mm
B	28mm
C	30mm
D	32mm
E	34mm

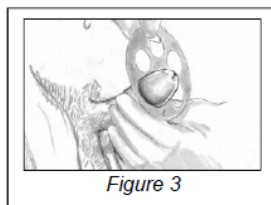


Figure 3

Note – If the diameter under the coronal sulcus is too large and cannot fit in the size E opening or if it is too small and cannot fit precisely to size P6, do not perform the PrePex procedure and refer the patient for surgical circumcision.

3. Prepare the skin with PI antiseptic solution:

- a. Soak one gauze in PI solution
- b. Retract the foreskin completely and use one soaked gauze to clean the whole penis starting from the glans to the sulcus, the inner and outer foreskin, and the penile shaft, the base of the penis and the scrotum. Clean well and remove all residual dirt using the PI solution, place extra emphasis on cleaning the inner foreskin and sulcus area (**Figure 4**). Once all debris has been removed, apply two more applications of PI waiting a short time between each application.
- c. Discard the used gauze while holding the penis with the free hand. (The penis should not come in contact with the body to avoid cross contamination).
- d. Situate the clean penis on a clean gauze, wait for 2 minutes allowing the Povidone Iodine to effectively disinfect the skin.
- e. Dry the penis with a gauze after completing the 3 Povidone iodine applications and waiting 2 minutes.

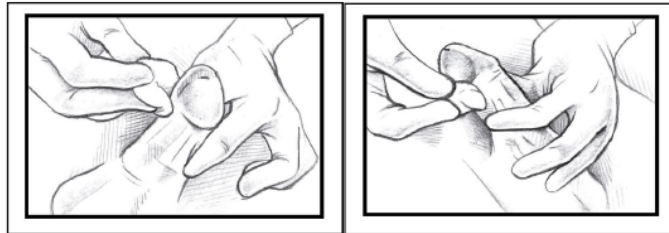


Figure 4 – Cleaning with PI the shaft, sulcus and inner foreskin

If the patient has a known allergy to iodine, use an alternative solution, such as chlorhexidine gluconate, following exactly the same disinfecting procedure described above.

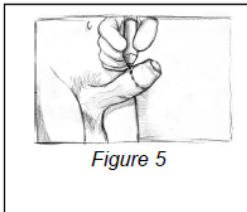


Figure 5

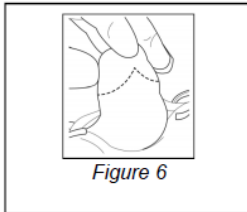


Figure 6

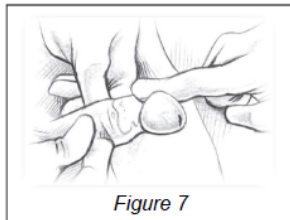
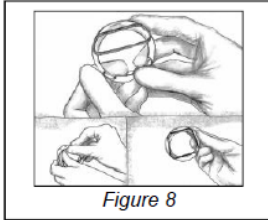


Figure 7

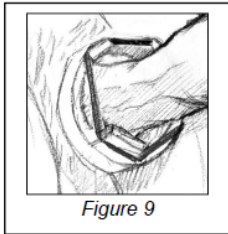
4. Mark the outer circumcision line according to the WHO Manual for Male Circumcision Under Local Anesthesia⁵ (Chapter 5-15 and Fig 5.17; Chapter 5-27 and Figs 5.33/5.34) using a standard medical skin marker (**Figure 5**).
5. This step is common to all methods of circumcision. Stretch the foreskin past the glans and release. When the foreskin has returned to a natural “resting” position, indicate the intended line of the circumcision with a skin marker. The line should correspond with the corona, just under the head of the penis. Some uncircumcised men have a very lax foreskin, which is partially retracted in the resting position. In such cases it is better to apply a little tension to the foreskin before marking the circumcision line. However, it is important not to pull the foreskin too hard before marking the line, as this will result in too much skin being removed.
6. Mark the intended circumcision line, as described above, with a V shape, pointed toward the frenulum, on the underside (ventral aspect) of the penis (**Figure 6**). The apex of the V should correspond with the midline raphe. Ensure the V shape is not too sharp.
7. Ensure that the marked circumcision line has not been erased during the PrePex procedure. If the marking is not clearly visible, do not perform the procedure. Before continuing, it is very important to mark the line again if necessary.

- Apply ~1 g of 5% anesthetic cream on the exposed shaft area up to the coronal sulcus (Figure 7). Once the anesthetic cream has been applied, there is no need to wait for the anesthetic cream to take effect and the procedure can commence immediately. Pull up the foreskin so the 5% anesthetic cream is covered by the inner foreskin

Placement Procedure:

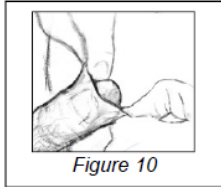


- Place the Elastic Ring on the Placement Ring (see Figure 8). Do not remove the Verification Thread; it is intended to correct Elastic Ring misplacement if needed.

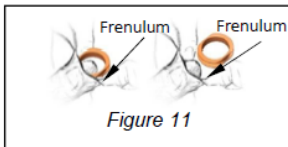


- Place the Placement Ring (with mounted Elastic Ring) on the penis shaft with the Elastic Ring distal to the body (See Figure 9).

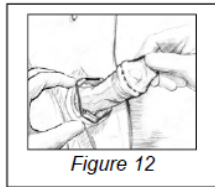
Steps 3 and 4 should be performed by 2 people.



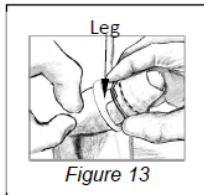
- Holding the foreskin dorsal and ventral sides, the first person should stretch the foreskin up and to the sides for insertion of the Inner Ring. Use fingers only with a dry gauze to enable a good grip; never use a tool of any kind to stretch the foreskin (See Figure 10). Ensure that the foreskin is fully stretched by viewing the sulcus area, thus assuring there will be no double entrapped foreskin.



- The second person should insert the Inner Ring with its flat parts toward the dorsal and ventral penis sides into the opening of the foreskin (see Figure 11), assuring that one of the flat sides is in the area of the frenulum and the other flat side is on the opposite side of the frenulum.



- Warning: When introducing the Inner Ring through the foreskin opening, take extra caution not to harm the foreskin. If it is hard to introduce the Inner Ring do not force it and do not perform the procedure.
- Introduce the Inner Ring over the glans and place it just below the glans (on the sulcus).
- Hold the foreskin closed at the tip of the penis to secure the Inner Ring in place (See Figure 12).



- Advance the Placement Ring and Elastic Ring toward the glans. Visually verify that the Elastic Ring surrounds with the Inner Ring groove and that the Elastic Ring and Inner Ring are aligned.
- Once the Elastic Ring and Inner Ring are aligned, support the Placement Ring with one hand, and with the other hand adjust the foreskin so the marked circumcision line is exactly aligned with the Elastic Ring. Adjust the foreskin from beneath each of the 4 Legs by gently pulling the foreskin downwards (See Figure 13).

- To place the Elastic Ring - Using 4 fingers of your dominant hand, hold the Elastic Ring and Inner Ring together in the

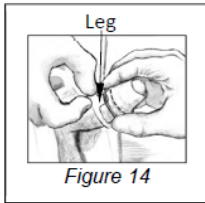


Figure 14

spaces between each of the 4 Placement Ring Legs. Work with the thumb and finger of your non-dominant hand to release the Elastic Ring from the Placement Ring one leg at a time (**Figure 14**).

10. Make sure the Elastic Ring is mounted directly over the Inner Ring groove and over the marked circumcision line previously marked. If the Elastic Ring is not positioned as desired or if a doubly entrapped foreskin is observed, use the verification thread to pull it off the penis and start the alignment procedure again.
11. Upon proper placement of the Elastic Ring, discard the Placement Ring, and cut the verification thread with the nurse utility scissors.
12. Supply the patient with 2 tablets of 400 mg Ibuprofen or other analgesic tablets, and post placement information.

Device Application: The following warnings must be provided to the patient prior to release:

- a. Do not move the device, even through clothes – emphasize that touching the device while urinating or bathing must not cause any movement of the device. Movement of the device may result in the need for surgical MC.
- b. Return for device removal after 7 days. Early removal may result in the need for surgical MC.
- c. Return to the MC center if the patient wants to remove the device before the 7 day period is over.
- d. Do not allow anyone other than a qualified PrePex provider remove the device.
- e. Report any unexpected situation, such as uncontrollable pain or device displacement.
- f. Do not pull on the foreskin in case of partial detachment.
- g. Abstain from sexual intercourse and masturbation when the device is on the penis, to avoid displacement.
- h. Do not place any non-medical substance on the penis or over the foreskin.
- i. Wear well-fitted underwear to hold the penis in an upright position.

Device Application: Inform the patient of the following prior to release

- a. The patient may experience pain in the following days, and should take the supplied analgesic tablets to control the pain.
- b. The foreskin distal to the Elastic Ring will become darker and dry.
- c. Unpleasant odor may occur while wearing the device.
- d. Infection may occur while wearing the device.
- e. There may be some partial skin detachments along the Elastic Ring.
- f. The patient should bath normally and keep the inner foreskin clean, while taking care not to dislodge or move the device.

Note: Special care should be taken while counseling adolescents under local laws and regulation

Removal Procedure:

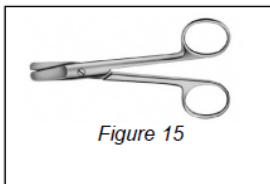


Figure 15

1. The device is removed 7 days after it has been placed.
2. It is mandatory to use only adequately sterilized removal tools. Using tools that have not been adequately sterilized, may lead to infection and/or contamination, particularly during the extraction of the Inner Ring when the spatula may come in contact with the patient's viable tissue. All removal tools require appropriate cleaning after use and before sterilization, or the sterilization process may not be effective.

3. It is recommended to use Harvey wire cutting scissors (**Figure 15**), due to their blunt edges and serrated blades, specifically designed to cut tough tissue like dried necrotic foreskin.
4. During the PrePex MC procedure, providers should wear examination gloves.

Foreskin Removal:

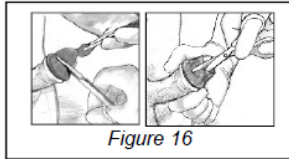


Figure 16

5. Before removing the foreskin it is recommended to pull the penis and foreskin gently upwards to separate the foreskin from the glans. You may drip fluids (e.g. water for irrigation) through the foreskin opening to enhance this separation and loosen the tissue.
6. If the opening of the foreskin is very narrow, it should be dilated very gently with the forceps tip to enable insertion of one of the wire scissors blades. Use sterile forceps to hold the foreskin and to pull it away from the glans.
7. Warning: When cutting the foreskin using wire scissors, take care that the foreskin is held far enough away from the glans and the meatus in order to avoid injury.
8. The foreskin should first be cut vertically towards the Elastic Ring and then at an angle, spirally, to the line that the Inner Ring is visible (**Figure 16**).
9. Cut the foreskin as close to the Elastic Ring as possible, the edge of the Inner Ring should become visible.

Elastic Ring Removal:

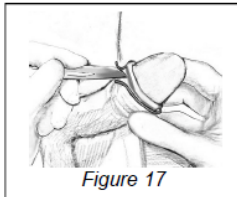


Figure 17

1. Warning: The Elastic Ring should be removed only after the foreskin has been removed.
2. Use a sterile scalpel to cut the Elastic Ring placed over the flat part of the Inner Ring on the side that is opposite to the frenulum. Never cut the Elastic Ring on the same side as the frenulum (**Figure 17**).
3. Take care not to harm the viable skin.
4. Discard Elastic Ring.

Inner Ring Removal:

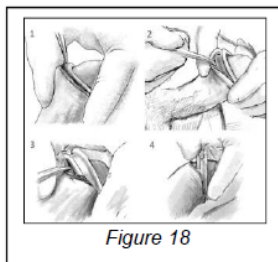


Figure 18

1. The Inner Ring is removed after the Elastic Ring removal. Before Inner Ring removal, thoroughly disinfect the area of the Inner Ring, the necrotic foreskin around it and the glans with PI and gauze, especially in the area where the spatula will be used. Use one gauze soaked with PI, clean well and remove all residual dirt using the PI solution. Once all debris have been removed, apply two more applications of PI solution waiting a short time between each application. Wait for 2 minutes before proceeding allowing the Povidone Iodine to effectively disinfect the skin. If the patient has a known allergy to iodine, use an alternative solution, such as chlorhexidine gluconate, following exactly the same disinfecting procedure described above.
2. Pull the Inner Ring out on a curved side using the spatula; take care to avoid the frenulum area (**Figure 18**), verify the spatula is properly sterilized.

3. Partial separation of the necrotic foreskin may occur; in such cases extra care should be taken when extracting the Inner Ring to minimize pain at the separation area.
4. After removal of the Inner Ring, it should be cut with scissors before discarding it.

Post Removal Procedure:

1. Clean the circumcised penis with PI solution, pay particular attention to the post removal wound area.
2. Dress the circumcised penis with a sterile non-adherent dressing with adhesive edges.

Removal: Inform the patient of the following prior to release

1. Instruct the patient not to wet the dressing.
2. Supply the patient with 4 new sterile non-adherent dressings with adhesive edges to take home. Instruct the patient that in case the dressing on the penis gets wet, he should remove it and replace it with a new, sterile dry dressing.
3. Instruct the patient to remove the dressing every day, at which time he can wash the penis and the wound area normally and then apply a new sterile dressing that has been supplied to him.
4. Instruct the patient to keep the wound dressed for at least 5 days, using the supplied dressings.
5. Instruct the patient to contact the MC clinic in case of pain, infection, swelling, drainage or fever. Inform the patient that all of those signs may occur following device removal and are an indicator for him to arrive to the MC clinic immediately.
6. Instruct the patient to abstain from sexual intercourse for 6 weeks after device removal and to avoid masturbation as these actions may lead to disruption of the wound, which will result in delayed healing.
7. Explain to the patient the importance of using condoms, and that circumcision is not a completely protective solution for the prevention of HIV infection.
8. Explain to the patient the risks associated with inappropriate wound care.
9. Educate the patient on the great risks and potential damage to the wound and to his general health if patients use traditional or non-authorized substances of any type over the wound (e.g., animal feces, organic substances, such as butter, powders, herbs, honey, etc.).

Note: Special care should be taken while counseling adolescents

Procedure and Device Associated Risks:

The following possible risks may occur while the patient is wearing the PrePex:

- Patient displacing the device from its original position may lead to pain and to diffused edema that will require surgical MC.

To mitigate such risk it is essential to explain to the patient that he should not move the device even if he has pain or discomfort, and he should not masturbate or have sex. In case of pain, the patient should take the supplied analgesic tablets. If the pain is uncontrollable, the patient should return to the MC center to be evaluated and clinically managed; early controlled removal of foreskin and device may be indicated. If there is displacement of the device with or without edema, the patient should return to the clinic as soon as possible where the provider may recommend surgical circumcision to avoid serious and possible life-threatening infection. Surgical circumcision should be performed within 6-12 hours after displacement.

The following possible risks may occur as a result of device misuse by the provider:

- If the Inner Ring is not located at the sulcus level, this may lead to disturbance of urine flow.
- If the Inner Ring is not pushed all the way down to the sulcus level this may lead to insufficient removal of foreskin.
- If the circumcision line is not marked according to recommendations presented in this document, this may lead to removal of excess foreskin and future problems with penile function, or to removal of insufficient skin.
- Penile injury during foreskin removal due to misuse of the wire scissors.

Other possible risks:

- Device displacement and edema requiring urgent surgical circumcision.
- Bleeding after device removal.
- Infection – such infections that are associated with anaerobic bacteria, such as *C. tetani* that may lead to tetanus.
- Delayed healing.
- Injury to the penis particularly during removal.
- Unpleasant odor while wearing the device.

It is important to report any complaint or incident occurring with the device to the manufacturer Circ MedTech, by email or phone as soon as possible.

Training:

To receive complete training materials, including presentations and videos, send an e-mail to info@prepex.com requesting the training material and a CD / flash drive will be sent as soon as possible.

Clinical Experience:

Clinical studies of PrePex were performed in Rwanda and Zimbabwe according to the WHO official Evaluation Framework of Adult Male Circumcision (MC) Devices.¹

Rwanda Studies:

1. A study that demonstrated the safety and efficacy of the PrePex device in 105 male subjects.² Results: All subjects achieved circumcision with 1 case of diffuse edema after device removal, which resolved with minimal intervention. There were no instances of erroneous placement and no mechanical problems with the device. Conclusion: The PrePex device was found to be safe and effective.
2. Randomized controlled study, comparing the safety and efficacy of the PrePex in 144 adult male subjects to a surgical circumcision method in 73 adult male subjects.³ Results: There were no device-related adverse events. Healing time of the PrePex arm was longer than the surgical arm. Conclusion: PrePex MC, takes significantly less time than surgical, is as safe, does not require injections or sterile settings, and seems to be suitable for application by nurses.
3. A cohort field study demonstrating the safety and efficacy of the PrePex on 518 adult males when the procedure is performed by nurses.⁴ Results: All 518 subjects achieved complete circumcision. There were 5 AEs on 4 subjects (rate of 0.96%). AEs were moderate and were resolved with simple intervention. Conclusions: The study demonstrated that nurses can be easily trained to perform safe and effective circumcisions using the PrePex.





Zimbabwe Studies:

4. A safety study to determine the safety and efficacy of the PrePex device, a total of 53 devices were successfully deployed. There were no moderate to severe AEs, only 1 incident of early removal requested by the subject. The median time for complete healing was 42 days. The PrePex device in this study was found to be very safe for use in VMMC for the adult population in Zimbabwe.
5. A Randomized Controlled Trial Comparing PrePex to Forceps Guided Surgical Circumcision. Healthy, non-circumcised adult male volunteers were allocated into the PrePex device (n=160) or surgical arm (n=80). The AE incidence rate for the PrePex arm was 1.3%, there were no AEs in the surgical arm. The trial results demonstrate that the PrePex procedure is quick, efficient, and effective.

6. A one arm prospective study evaluating PrePex device in adults, when used by nurses. 603 adult males were enrolled. Results: 602 subjects (99.8% rate) achieved complete circumcision, there were 4 (rate of 0.7%) severe and moderate AEs, in four men. By day 56 all participants were declared fully healed. Conclusions: PrePex can be used safely by nurse providers in scale up of VMMC, associated AEs were low and reversible.
7. Safety and Efficacy of the PrePex device for male circumcision performed by primary care nurses (PCN). Results: 601 adult males were enrolled at 4 provincial health facilities, PCNs performed all procedures. 2 (rate of 0.3%) severe AEs were reported due to subject self-removal of the device. 99% of participants were completely healed by day 49. Conclusions: PrePex is safe for use by PCNs at all facility levels, even very rural settings.
8. One arm, open label prospective study using PrePex in men aged 13-17. Results: 402 men were included in the study in two age groups: 199 in the 15-17 group and 203 in the 13-14 group. The Moderate/Severe AE rate was 0.5%, mean healing time was 31.9 days. There was a high ineligibility rate (35.9%) mainly due to phimosis & preputial adhesions. Conclusions: PrePex device is safe and efficacious for MC scale up with adolescents. Low AE rate, lower pain scores and faster wound healing were observed compared to adult PrePex circumcision

References:

1. World Health Organization. Framework for Clinical Evaluation of Devices for Adult Male Circumcision. Geneva, Switzerland; WHO; September 2012.
2. Bitega JP, Ngeruka ML, Hategekimana T, Asimwe A, Binagwaho A. Safety and efficacy of the PrePex device for rapid scale up of male circumcision for HIV prevention in resource-limited settings. *J Acquir Immune Defic Syndr.* 2011;58: e127-134.
3. Mutabazi M, Kaplan SA, Rwamasirabo E, Bitega JP, Ngeruka ML, Savio D, Karema C, Binagwaho A. HIV Prevention: Male Circumcision Comparison Between a Nonsurgical Device to a Surgical Technique in Resource-Limited Settings: A Prospective, Randomized, Nonmasked Trial. *J Acquir Immune Defic Syndr.* 2012; 61: e49-55.
4. Mutabazi V, Kaplan.S.A, Rwamasirabo E, Bitaga JP, Ngeruka M.L, Savio D. One-Arm, Open-Label, Prospective, Cohort Field Study to Assess the Safety and Efficacy of the PrePex Device for Scale-Up of Nonsurgical Circumcision When Performed by Nurses in Resource-Limited Settings for HIV Prevention. *J Acquir Immune Defic Syndr.* 2013; 63: 315-322
5. World Health Organization. Manual for Male Circumcision Under Local Anesthesia, Geneva, Switzerland; WHO; version 3.1.December 2009.

			
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