Female condom technology: new products and regulatory issues

Mags Beksinska, Jenni Smit, Carol Joanis, Margaret Usher-Patel, William Potter

Maternal, Adolescent and Child Health (MaCH), Department of Obstetrics and Gynaecology, University of the Witwatersrand, Overport 4091, South Africa

Joanis Consulting, Raleigh, NC 27613, USA

World Health Organization, Special Programme of Research, Development and Research Training in Human Reproduction, Department of Reproductive Health and Research, World Health Organization, CH 1211 Geneva 27, Switzerland

WD Potter, Stapleford Scientific Services Ltd., Madeline House, High Street, Babraham, CB22 3AG Cambridge, UK

Received 11 July 2010; revised 21 July 2010; accepted 21 July 2010

Abstract

Like male condoms, female condoms (FCs) provide protection against unplanned pregnancy and most sexually transmitted infections including HIV. The first FC made by the Female Health Company was approved by the US Food and Drug Administration (USFDA) in 1993. Since 2000, several different types of FCs have become available or are in development to lower the cost and/or improve acceptability. Although similar in function, new FCs often differ in design and materials. Classified as Class III medical devices by the USFDA, FCs have a regulatory process that is more complex than that for male condoms. This, coupled with the lack of an international standard to verify the quality of new devices, has hindered new products gaining regulatory approvals and entering the market. We review the existing regulatory pathway for FCs, the progress made in developing standards specifically for FCs and the FCs available now or in development, including their current status regarding approval.

© 2010 Elsevier Inc. All rights reserved.

Keywords: Female condoms; Regulatory process; Standards; Prototypes

1. Introduction

The first female condom (FC) made by the Female Health Company (FHC) was approved by the US Food and Drug Administration (USFDA) in 1993. Since 2000, new FCs have become available or are in development to lower the cost and/or improve acceptability. As new products enter the market, there is a need to address a number of research and regulatory issues. The International Organization for Standards (ISO) is a worldwide federation of national standards bodies and experts, responsible for drafting international standards based on the best available evidence and practice. ISO has developed a clear, generic standard for male natural rubber latex (NRL) condoms which provides essential guidance on the design and safety of male condoms and specifies the performance requirements and the tests required for verification of the quality of these devices. The international standard for FCs is in the final stages of development. Given the number of possible FC designs and different materials that could be used in their construction, the standard will not be generic (i.e., it will not be specific with respect to requirements for certain properties such as dimensions and strength). Instead, it will require manufacturers to conduct clinical studies to verify the contraceptive effectiveness and performance of any new or modified FC design. However, contraceptive effectiveness studies may be waived in instances where the new device is similar in specifications, testing requirements and design to an existing marketed device. In this case, a performance (failure rate) study may be acceptable, subject to certain conditions. Manufacturers will also be required to base the specifications for these products on the properties of the FCs used in these trials.

Without an existing standard, the effectiveness and safety of each FC design have to be evaluated by experts on an individual basis. Donors purchasing condoms as part of international aid programs may require endorsement of the World Health Organization (WHO) or approval by the USFDA if a new FC is to be considered for procurement. In order to ensure safety and quality requirements and make
recommendations for bulk procurement, the WHO, Department of Reproductive Health and Research (RHR), at the request of the United Nations Population Fund (UNFPA) established a Female Condom Technical Review Committee in 2006 to assess the quality of the products for bulk procurement [1]. This is an ongoing review process conducted by an expert group and based on the WHO/UNFPA prequalification procedure used for male natural latex condoms. At present, only the FC1/FC2 FCs have fully completed the review process and been approved for public sector distribution. During the review process, the committee defined and published a list of FC failure modes [2]. These definitions have since been updated and are listed in Appendix A, and should be applied in conjunction with a specific risk assessment for the clinical assessment of the FC.

2. Female condoms available now or in development

Existing and new designs of FCs are made from NRL, synthetic latex (nitrile) and polyurethane. Although different FCs often have unique design features, there are similarities between them with respect to function. All FCs require an anchor outside the vagina to prevent invagination (i.e., being pushed inside the vagina during use). This feature, usually a ring or frame, is also used for removal. A mechanism for inserting the device and stabilizing it once fitted is also required. The following section describes the different FCs that are available now or are still in development and will be available within the next 2 to 5 years.

2.1. The FC1 female condom

This condom, made by the FHC, was the first FC available and was marketed under various brand names including Reality®, Femy®, the Care Contraceptive Sheath® and Femidom® (Fig. 1). The FC1 is an effective contraceptive if used consistently and correctly. It is estimated that about 5% of women who use this FC consistently and correctly will become pregnant over the first year of use and this rises to 21% in those who do not use it correctly. Production of FC1 ceased at the end of 2009 [3–5]. It has now been replaced with the FC2® FC.

As FC1 has a 5-year shelf-life, existing supplies may still be available for several years. FC1 was made by die-cutting polyurethane material — a labor-intensive and expensive process. Polyurethane is odorless, rarely causes allergic reactions and, unlike latex, may be used with both oil-based and water-based lubricants. It is 170 mm in length and has a flexible inner ring to insert the device and keep the condom in place during sexual intercourse. A ring at the open end of the condom lies flat across the genital area and further ensures that the condom stays in place. In addition to USFDA approval, this condom has European Union (EU) approval and the CE Mark.1 As the FC1 was first to enter the market, there is a body of research published on its contraceptive efficacy [3–5], acceptability [6], function [7–9] and sexually transmitted infection (STI) prevention effectiveness [10].

2.2. The FC2® female condom

The FC2 FC made by the FHC became available in some countries in 2005. This FC has completed the technical review process by the WHO, which found it acceptable for bulk procurement by all UN agencies in 2007 [1]. In 2009, it was approved by the USFDA. This condom is similar in specification, function and appearance to the original FC1 polyurethane condom but is made of synthetic nitrile rubber latex (Fig. 2) and does not have a seam.

Synthetic nitrile rubber latex is a terpolymer of butadiene, acrylonitrile and methacrylic acid, commonly referred to as nitrile rubber, which is widely used for making medical examination gloves. FC2 is manufactured by a dipping process on high-volume automated production lines which makes this FC cheaper to produce compared to the polyurethane FC1. The effectiveness and acceptability of FC2 have been found to be comparable to the polyurethane FC1 FC [4,11]. In these studies, no difference was found in failure rates such as breakage, slippage and invagination. There are no data available to date on efficacy for pregnancy and STI prevention of the FC2 FC. Approval was granted by the USFDA on the basis of non-inferiority in functionality of FC2 compared to FC1 and that the design and specifications of the two condoms were similar.

Fig. 1. The FC1 female condom.

1 A certification given when a product fulfils the European Union safety, health and environmental requirements.
2.3. The VA w.o.w® Condom Feminine female condom

The VA w.o.w® (worn of women) Condom Feminine® or L’amour (Medtech Products, Ltd., Chennai, India) is also known as the Reddy FC, after the name of its designer. This FC is made of NRL, the same material as male condoms, and encases a medical-grade sponge at the closed end of the device. The sponge is used for insertion and the condom is 90 mm in length. The outer anchoring structure takes the form of a triangular-shaped frame (Fig. 3). This frame serves the same purpose as the outer ring of the FC1 and FC2. It comes lubricated with silicone oil. If additional lubricant is needed, only water- or silicone-based lubricants can be used. In a study conducted in India, this condom was found to be acceptable to users [12]. There are no available effectiveness data for this FC.

The VA w.o.w® FC has received approvals from the EU, the India Drug Control Authority and the Ministry of Health in Brazil, and carries the CE Mark. This FC is still under review by the WHO pending data from a final clinical trial to be undertaken in 2011 to provide more data to the WHO/RHR Female Condom Technical Review Committee and to regulatory bodies.

2.4. The Woman’s Condom

The Woman’s Condom (WC) is made of polyurethane and is inserted using an insertion capsule. The condom sheath, which is 227 mm long, is tucked into the capsule which dissolves after insertion (Fig. 4) releasing the condom within the vagina. The dissolving capsule is made of polyvinyl alcohol, the same material used to make C-film which is a spermicidal contraceptive in the form of a solid plastic film inserted into the vagina. The four foam dots on the body of the condom are hydrophilic and cling lightly to the vaginal wall to ensure stability. The condom is not pre-lubricated and can be used with oil- or water-based lubricants.

WC will be marketed with a sachet of water-based lubricant. Although not yet commercially available, acceptability trials have shown the WC is acceptable to users [13–14]. Effectiveness data studies are planned and will be conducted within the next 2 years. This device was transferred to a Chinese manufacturer (Shanghai Dahua Medical Apparatus Co., Ltd.) in 2008, and data from a trial currently underway in China will be submitted towards an application for Chinese State Food and Drug Administration (CSFDA) approval in 2010, followed by CE marking. Further trials are planned to commence in 2010 that will be submitted for review by the WHO/RHR Female Condom Technical Review Committee and USFDA approval.

2.5. The Phoenurse female condom

The Phoenurse FC is produced and distributed in China (Condombao Medical Polyurethane Co. Ltd., Shanghai, China). It is made of polyurethane and comes with an
insertion tool, a water-based lubricant, sanitary towel and a disposal bag (Fig. 5). The body of the condom is slightly longer than the FC1/FC2 at 180 mm and is dumbbell shaped. It also has an inner ring and outer ring. The Phoenurse FC has Chinese SFDA approval but is not sold outside of the country. A recent trial in China found that the condom is acceptable to women and its functional performance for FC failure modes is similar to FC1 [15].

2.6. The Cupid® female condom

The Cupid FC (Cupid Ltd., Mumbai, India) is a new design and is manufactured and available in India and some European countries. This FC is made of NRL with an octagonal outer frame (Fig. 6). The condom is 155 mm in length and is inserted using a sponge which also holds the condom in place during use. The condom is pre-lubricated with silicone oil and comes in both natural and pink colors. It is the only FC that is scented. It currently holds the CE mark and is registered by the India Drug Control Authority. This FC is under review by the WHO/RHR Female Condom Technical Review Committee, and some unpublished technical reviews and pilot clinical work indicate that this may be an acceptable device. Further clinical trials will be undertaken in the next year to provide more data to the WHO/RHR Female Condom Technical Review Committee and to regulatory bodies.

2.7. Panty female condoms

Panty FCs have a distinct design compared to other FCs. The panty performs the same function as the outer ring or frame of the FCs mentioned earlier in this section. These FCs cannot be used without the reusable panty and a new condom sheath must be inserted, secured into the panty and removed after each use. Panty FCs are more expensive than the non-panty varieties and are generally less available.

3. Conclusion and recommendations

Male and female condoms are currently the only effective dual protection against unintended pregnancy and the transmission of STIs, including the human immunodeficiency virus (HIV) that causes AIDS [16]. This article has discussed several devices and there are several more in the pipeline in various stages of development. However, funding for the development of new condom technology is virtually non-existent. Male condoms are designated as Class II medical devices by the USFDA, while FCs are considered Class III. Class III status was applied to FCs for safety reasons as there was no previous history of FC contraceptive effectiveness; however, this means that new FCs entering the market are subject to more stringent requirements in the US and other regulatory approval processes than are male latex condoms. Clinical trials addressing contraceptive and/or STI/HIV prevention effectiveness of new FCs are prohibitive in cost and take years to complete. In Europe, for CE marking, FCs are in the same class as male condoms (Class IIb). Whereas there is a harmonized European standard (EN / ISO 4074) for male condoms, there is no standard yet for FCs. This means that even though male condoms and FCs are in the same class, more clinical evidence is required to get CE Mark clearance for FCs.

Thus, getting a new FC through some regulatory processes and into the market is highly challenging. Today, the number of manufacturers willing and able to take on the financial
investment and lengthy process from product design to final approval is limited. As a result, acceptable alternatives to contraceptive and STI efficacy trials are being explored [17] and the potential for using semen biomarkers may be considered in the future. In spite of the difficulties faced in bringing new FCs to market, there has been a resurgence of interest in FC technology as evidenced by the emergence of several new innovative designs by manufacturers from a range of countries. These manufacturers urgently need more support and guidance to enable them to undertake all the required research and development, quality assurance testing and clinical trials required to produce quality products and compile the required documentation needed for country regulatory and bulk procurement approvals. To assist manufacturers interested in designing/manufacturing new FCs, UNFPA and WHO/RHR are planning to hold a workshop to take all interested parties through the requirements from research, design, development, safety, efficacy, regulation, promotion and procurement. In addition, WHO/RHR will work with UNFPA to develop a prequalification system and the Universal Access to Female Condoms Joint Programme (UAFC) is sponsoring research to assist selected FC manufacturers with the clinical research necessary to obtain WHO pre-qualification. 

Renewed interest in the FC, emergence of a variety of new FC designs, and initiatives to facilitate new FCs through the regulatory process are promising moves towards increasing options for providing a woman-controlled device that has the potential to protect against unwanted pregnancy and disease acquisition.

Acknowledgments

We would like to acknowledge the William and Flora Hewlett Foundation for support to authors Beksinska and Smit.

Appendix A. Female condom failure modes

A risk assessment for the product shall be conducted in accordance with ISO 14971. The assessment shall identify all potential failure modes for the device as well as any other safety and efficacy concerns. Failure modes identified in the risk analysis will be compared to the list of known female condom failure modes. In addition to these known failure modes, any new failure modes shall be assessed in the design and execution of any pre-clinical or clinical investigations of the female condom. Manufacturers shall make the results of the risk assessment available to regulatory authorities.

The following are definitions of known female condom failure modes.

(a) Clinical breakage is defined as breakage during sexual intercourse or during withdrawal of the female condom from the vagina. Clinical breakage is breakage with potential adverse clinical consequences. The clinical breakage rate is calculated by dividing the number of female condoms reported to have broken during sexual intercourse or during withdrawal by the number of female condoms used during sexual intercourse.

Total breakage is defined as the sum of all female condom breakages at any time before, during or after sexual intercourse. It includes both clinical breakages and non-clinical breakages. The total breakage rate is calculated by dividing the total number of female condoms that broke by the number of female condom packages opened.

(b) Slippage is defined as an instance when a female condom slips completely out of the vagina during sexual intercourse. The slippage rate is calculated by dividing the number of female condoms that slipped by the number of female condoms used during sexual intercourse.

(c) Misdirection is defined as vaginal penetration whereby the penis is inserted between the female condom and the vaginal wall. The misdirection rate is calculated by dividing the number of reported events of misdirection by the number of female condoms used during sexual intercourse.

(d) Invagination is defined as an instance when the external retention feature of the female condom is partially or fully pushed into the vagina during sexual intercourse. The invagination rate is calculated by dividing the number of events of invagination by the number of female condoms used during sexual intercourse.

Total clinical failure is defined as the sum of female condoms that clinically break or slip, or are associated with misdirection, invagination or any additional failure modes(s) identified in the risk assessment which results in the reduction of the female condom protective function. The total clinical failure rate is calculated by dividing the number of female condoms with a clinical failure by the number of female condoms used during sexual intercourse.

Total female condom failure is defined as a female condom for which a non-clinical breakage, clinical breakage or slippage occurs, or is associated with misdirection, invagination or any additional failure modes(s) identified in the risk assessment. The female condom failure rate is calculated by dividing the number of female condoms that fail by the number of female condom packages opened.

References


