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Female Condom Updates

Development and Approval of New Female Condom Designs: Negotiating the Regulatory Process By Mags Beksinska (CBAS steering committee member) and Bill Potter

Male latex condoms have a long history of safety and effectiveness, and their performance during use is well established. However, far less information is available for female condoms (FCs). There is limited research on FC functionality and in many published studies to date events such as breakage and slippage are based on equivalent definitions for male condoms. However, we now know that failure modes for FCs (aside from breakage) are more complex and have only recently been better understood and described (Beksinska et al. 2007, WHO Technical Review Committee 2007). Clinical trials collecting data on FC functionality need to ensure that the correct terms and definitions are used.

Since the approval by the United States Food and Drug Administration (USFDA) of the first FC (FC1) in 1992, several different types of FCs have become available or are in development to lower cost and/or improve acceptability. FC2, the second-generation female condom made by the Female Health Company, was approved by the USFDA in early 2009 and will replace FC1. FC2 is made from a synthetic latex whereas FC1 is made from polyurethane, though both products have essentially the same design. Other new designs of FCs are made from natural latex, synthetic latex, and polyurethane. These new designs and new materials require clinical validation to ensure that their performance during actual use is not inferior to that of currently approved FCs.

The International Organisation for Standards (ISO) is a worldwide federation of national standards bodies responsible for drafting international standards based on the best available evidence and practice. It has developed a clear standard for male condoms and this provides essential guidance on specifications and test methods used to verify the quality of male condoms. The international standard for FCs, which will be published as ISO 28541, is still under preparation, meaning there is currently no generic specification. The ISO standard is now in the final stages of development and could be published as early as next year. Given the large number of possible FC designs and different materials used, the standard will not be generic in the sense of specifying requirements for properties such as dimensions and strength. Instead it will require manufacturers to verify the effectiveness of any new or modified FC design by clinical studies. Manufacturers will also be required to base the specification for the product on the properties of the condoms used in the trial.

Without regulatory approvals, many FC manufacturers cannot enter the market and be considered for procurement by donor agencies. Male condoms are designated as Class II medical devices (requiring special controls like product labeling) by the USFDA while the FC is considered Class III (requiring premarket clinical trials in addition to special controls). This was done for safety reasons as there was no previous history of FC effectiveness. It also means that new FCs wanting to enter the market are subject to far more stringent requirements in regulatory approval processes, including clinical evaluation.

Currently the effectiveness and safety of each FC design has to be evaluated by experts on an individual basis. The World Health Organization (WHO) established a Female Condom Technical Review Committee in 2006. This expert group was convened to evaluate FC manufacturers' dossiers in order to make recommendations for bulk procurement of FCs that met a set of predetermined performance, safety, and quality requirements. Emerging FC manufacturers urgently need more guidance to enable them to undertake all the required testing and compile the required documentation needed for regulatory approvals. The publication of ISO 28541 will greatly assist in meeting this objective and ISO is now working on a standard to provide guidance on the design, execution, and analysis of clinical trials on FCs. The process of getting the clinical trial guidance and standards for FCs is being supported by the WHO, USFDA, ISO, and experts in the field. Although there is still some way to go, the path to getting new FC designs through manufacturing, into production, and through regulatory approval is becoming clearer.

References

- Beksinska M, Joanis C, Manning J, Smit J, Callahan M, Deperthes B, Usher-Patel M. Standardized definitions of failure modes for female condoms: A Commentary. *Contraception* 2007; 75:251-5.
- WHO. Female condom technical review committee: Report of a review committee. 2007. Available here: <u>http://whqlibdoc.who.int/hq/2007/WHO_RHR_07.18_eng.pdf</u>.

New CBAS Female Condom Bibliography

We are excited to share this new resource with the CBAS community. Our bibliography of the literature on the female condom includes the latest peer-reviewed, published articles through May 2010. You can download the bibliography from our website with the articles listed chronologically (www.cervicalbarriers.org/documents/ FemaleCondomBibliography23_June_10CHRONORDER.pdf) or alphabetically by first author (www.cervicalbarriers.org/documents/ FemaleCondomBibliography23_June_10ALPHAORDER.pdf).



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Universal Access to the Female Condom Programs Launched in Cameroon and Nigeria

In our March newsletter last year, we featured an article about the exciting collaboration between Oxfam Novib, the World Population Foundation, IDA Solutions, and the Netherlands Ministry of Foreign Affairs: the Universal Access to the Female Condom (UAFC) Joint Programme. UAFC aims to make female condoms widely available through the support of various activities, including advocacy, programming,

and research. The initiative has recently launched programs in Cameroon and Nigeria; you can find more information on these program activities on the UAFC website: www.condoms4all.org/section/9/Country_programmes. Also, visit http://www.youtube.com/watch?v=65kYjCyTedA and www.youtube.com/watch?v=L150dKns1Ac to watch two video clips created for the Cameroon program by a collective of famous African musicians, among them Manu Dibango, promoting the female condom.



Female Condom Advocacy and Access in the United States

Since the USFDA approval in 2009 of the FC2, the Female Health Company's second generation female condom, various cities across the United States have launched initiatives to increase awareness of and

expand access to female condoms. The FC2 is being distributed for free in Washington, DC, by the Department of Health; in Chicago by the Chicago Female Condom Campaign, "put a ring on it;" and in New York City by the Department of Health and Mental Hygiene. Please see the FC2 website for more information about these campaigns: www.fc2.us.com/cityprograminformation.html. Also of interest, the Center for Health and Gender Equity (CHANGE) held a speaker's panel at the 54th Commission on the Status of Women on March 9, 2010, promoting advocacy for female and male condoms. Find out more about the event at:



www.preventionnow.net/news_and_events/events /female_male_condoms_at_csw/.

Featured Research

The following are published abstracts of research studies on topics related to cervical barrier methods.

Multipurpose prevention technologies for sexual and reproductive health: Gaining momentum and promise. Holt BY, Kilbourne-Brook M, Stone A, Harrison P, Shields WC. *Contraception.* 2010;81(3):177-80.

Editorial summary: *Current prevention strategies have largely focused on a single health outcome, which does not adequately address the link between unplanned pregnancy and STIs. Multipurpose prevention technologies have the potential to meet multiple sexual and reproductive health needs.*

Adding to the menu of modern methods – the diaphragm. Holmes W. Sexual Health. 2010;7:101-102.

Editorial summary: Although not suitable for all, many women in low-income settings could benefit if they were able to choose the diaphragm, especially a one-size-fits-all version. Research is needed to establish efficacy when the diaphragm is used continuously and without spermicide.

State-of-the-art of non-hormonal methods of contraception: I. Mechanical barrier contraception.

Batár I, Sivin I.

The European Journal of Contraception and Reproductive Health Care. 2010;15:67–88.

Mechanical barriers, specifically male condoms, command renewed interest and are used today by more people. The worldwide prevalence rate of male condoms was about 6% in 2007 corresponding to 65 million cohabiting couples. The prevalence of female barrier methods, including diaphragms, cervical caps and female condoms, has declined to less than 1% of women in North America and in northwest Europe. Even smaller percentages use female barriers elsewhere. First-year life table pregnancy probabilities of mechanical barrier methods range from 4 to 19 per hundred in clinical trials. The male condom is the only proved preventive tool against several sexually transmitted infections (STIs), especially HIV. The effectiveness of the diaphragm and cervical caps in this regard appears limited. Further research is needed to measure the efficacy of female condoms in disease prevention. Sponges are not known to protect against STIs. Because of their ease of use and availability, low short-term costs, relative freedom from side effects, and usefulness in combating STIs, mechanical barrier methods, especially condoms, will continue to be used on a large scale. For our literature search we used personal files, search engines such as Popline, Medline, PubMed and Google, and databases of WHO, FHI and Cochrane Library.

State-of-the-art of non-hormonal methods of contraception: II. Chemical barrier contraceptives. Batár I.

The European Journal of Contraception and Reproductive Health Care. 2010;15:89-95.

Chemical contraceptives mainly known as spermicides are one of the oldest types of contraceptives. The industrial revolution facilitated new developments, and they became a leading and widespread method. However, their use declined in the second half of the 20th century, and came under focus again only with the upsurge of sexually transmitted infections (STIs). The effectiveness of spermicides depends on the users' compliance and pregnancy rates vary widely: from 6/100 woman-year (with perfect use) to 26/100 woman-year (with typical use). Preparations consist of two components: an excipient (foam, cream, jelly, soluble film, suppository or tablet); and a chemical agent with spermicidal properties (acidic compound, microbicidal agent, detergent). The most widely used active agent has been the surface active (detergent) nonoxynol-9 (N-9). Based on their mode of action (surfactant effect of detergents, enzymatic action of microbicides on cell metabolism) spermicides were thought to provide protection against STIs including HIV. Recent studies have, however, shown that detergents may actually increase the risk. Because of this, there is an urgent need for a suitable nondetergent spermicide, and research should focus on developing new compounds to replace N-9 and other agents having similar undesired effects. This paper reviews the latest studies reporting results on these recent developments.

Results of a safety and feasibility study of the diaphragm used with ACIDFORM Gel or K-Y® Jelly.

von Mollendorf CE, Van Damme L, Moyes JA, Rees VH, Callahan MM, Mauck CK, Puren AJ, Tweedy K,

Taylor D. Contraception. 2010;81(3):232-239.

Background: New strategies are needed for preventing HIV infection in women. One potential approach is female-initiated use of an effective topical microbicidal gel in combination with a cervical barrier such as the diaphragm. Study design: Randomized, placebo-controlled safety and feasibility trial of diaphragm with vaginal gel during 6 months of use among 120 HIV-negative sexually active women in Johannesburg, South Africa. Results: Pelvic event rates were 338.3 and 247.1 per 100 women-years in the ACIDFORM gel (plus diaphragm) and K-Y[®] Jelly (plus diaphragm) groups, respectively, with a rate ratio of 1.37 (95% CI: 0.89-2.11). Most women found diaphragm with gel use acceptable. Conclusion: There was a trend towards more safety events in the ACIDFORM plus diaphragm group, although no primary comparisons achieved statistical significance. Adding an effective microbicidal gel to a mechanical barrier may still prove to be an important and acceptable combination method to help prevent pregnancy and HIV/sexually transmitted infection transmission. Background: Women have been regularly underestimated in their ability to care for and wear cervical barrier devices such as diaphragms appropriately. Methods: Data from two nonrandomised, non-blinded, non-significant risk acceptability studies of a novel cervical barrier device, the SILCS diaphragm, conducted in the Dominican Republic (n = 20), South Africa (n = 20)21) and Thailand (n = 20), are used to provide insights into the fundamental question of how women actually use an intravaginal device within the constraints of low-resource settings. In all sites, couples not at risk of pregnancy and at low risk of sexually transmissible infections used the SILCS diaphragm four times and provided feedback on acceptability, care and use of the device via product use questionnaires and genderspecific debriefing interviews. Results: Data from

user acceptability studies in these three countries provide an intimate view of how women care for and store the SILCS diaphragm, and both female and male perceptions about handling and re-using it. Results support the view that women are able to wear and care for diaphragms successfully in a variety of settings. In general, male partners were also supportive of care and reuse of the diaphragm. Conclusions: While the results from these studies indicate that women are able to find ways to cope successfully with the logistics of wearing and caring for an intravaginal device, further supportive evidence from a womancentred perspective is crucial for reproductive health policymakers and program managers. The authors contend that it is time to reassess perceived constraints to barrier protection.

Vaginal practices and associations with barrier methods and gel use among sub-Saharan African women enrolled in an HIV prevention trial. Van der Straten A, Cheng H, Chidanyika A, De Bruyn G, Padian N, MIRA Team. *AIDS Behavior*. 2010;14(3):590-9.

Vaginal practices may interfere with the use and/ or the effectiveness of female-initiated prevention methods. We investigated whether vaginal practices differed by randomization group in a phase III trial of the diaphragm with lubricant gel (MIRA) in Sub-Saharan Africa (n = 4925), and if they were associated with consistent use of study methods. At baseline, vaginal practices were commonly reported: vaginal washing (82.77%), wiping (56.47%) and insertion of dry or absorbent materials (20.58%). All three practices decreased during the trial. However, women in the intervention group were significantly more likely to report washing or wiping during follow-up compared to those in the control group. Additionally, washing, wiping, and insertion were all independently and inversely associated with consistent diaphragm and gel use and with condom use as well, regardless of study arm. A better understanding of the socio-cultural context in which these practices are embedded could improve educational strategies to address these potentially modifiable behaviors, and may benefit future HIV prevention interventions of vaginal methods.

A crossover comparison of two types of female condom. Hou LY, Qiu HY, Zhao YZ, Zeng XS, Cheng YM. International Journal of Gynecology and Obstetrics. 2010;108(3):214-218.

Objective: To compare the performance and acceptability of 2 types of female condoms (FCs) among female sex workers (FSWs) in China. Methods: The present crossover survey trial was conducted in Enping City between September and December 2007. Results: There were no significant differences between the 2 types of condoms in cumulative rates of episodes of misdirection; participants experiencing discomfort or feeling the outer or inner ring of an FC; or the clinical breakage or turning inside out of an FC. The rates of total clinical failures were similar for both FC types. Moreover, 59.5% of the survey participants reported that either type was acceptable to them. Conclusion: There were no statistically significant differences in performance between the 2 types of FCs tested, and most participants would accept using either in the future. Barriers to diaphragm use: The views of advanced nurses. Kulczycki A, Qu H, Bosarge PM, Shewchuk RM. Journal of Family Planning and Reproductive Health Care. 2010;36(2):79-82.

Background and Methodology: Women have used the contraceptive diaphragm for decades. Although use has recently declined, the diaphragm may find a new role in STI/HIV and dualprevention programmes when microbicides become available. We developed a questionnaire to examine seven provider issues identified as possible barriers to diaphragm use among advanced practice nurses (APNs) specialising in women's health. The perceived degree to which each issue represented a barrier was examined. Non-parametric correlations were calculated between diaphragm fitting history, demographic and practice characteristics, and the response ratings for each issue. Results: Responses were analysed for 204 APNs who averaged 15 years' experience in women's health care; 87% had fitted a diaphragm at least once, but 40% had not prescribed one in the past year. The degree to

which each issue was perceived as a barrier varied. Based on respondents' ratings of a 'more than moderate barrier,' diaphragm non-promotion by women's health providers, effectiveness doubts, unfamiliarity and lack of access to educational materials were more often perceived as impeding diaphragm use. Other results indicated that APNs with recent diaphragm fitting history perceived five of the seven issues to be less of a barrier: nonpromotion by women's health providers, lack of access to educational materials and to a fitting set, unfamiliarity, and inadequate reimbursement. Discussion and Conclusions: Formulation of successful strategies to reintroduce the diaphragm will depend on better identification and understanding of provider-perceived barriers. This paper offers new insights about such barriers and guidance for the development of strategies for diaphragm reintroduction.

Weighing the gold in the gold standard: Challenges in HIV prevention research. Padian NS, McCoy SI, Balkus JE, Wasserheit JN. *AIDS*. 2010;24(5):621-635.

Objective(s): Few HIV prevention interventions have been evaluated in randomized controlled trials (RCTs). We examined design, implementation, and contextual considerations that may limit detection of a positive or adverse effect in HIV prevention trials. Design: A systematic review of late phase RCTs for prevention of sexual transmission of HIV that randomly allocated intervention and comparison groups; evaluated interventions to prevent sexual transmission in nonpregnant populations; and reported HIV incidence as the primary or secondary outcome. Methods: PubMed/MEDLINE, other electronic databases, and electronic conference proceedings of recent HIV/AIDSrelated conferences were searched to identify published or unpublished trials meeting the inclusion criteria. Descriptive, methodological, and contextual factors were abstracted from each trial. Results: The review included 37 HIV prevention

RCTs reporting on 39 unique interventions. Only six RCTs, all evaluating biomedical interventions, demonstrated definitive effects on HIV incidence. Five of the six RCTs significantly reduced HIV infection: all three male circumcision trials, one trial of sexually transmitted infection treatment and care, and one vaccine trial. One microbicide trial of nonoxynol-9 gel produced adverse results. Lack of statistical power, poor adherence, and diluted versions of the intervention in comparison groups may have been important issues for the other trials that demonstrated 'flat' results. Conclusion: Almost 90% of HIV prevention trials had 'flat' results, which may be attributable to trial design and/or implementation. The HIV prevention community must not only examine evidence from significant RCTs, but must also examine flat trials and address design and implementation issues that limit detection of an effect.

Featured Recent Conferences

Women Deliver 2010

The second Women Deliver conference was held in Washington, DC, June 7-9, 2010. The theme was:

"Delivering solutions for girls and women," with a focus on political, economic, social/cultural, and technological solutions. Women Deliver 2010 had two strong messages:

- The MDGs will not be achieved without investing in women.
- There is just enough time, if the world commits funding now, to achieve MDG5 with an additional US\$10 billion annually by 2010 and US\$20 billion annually by 2015.

Kelly Blanchard of Ibis Reproductive Health and Serra Sippel of CHANGE moderated a session entitled "Prevention solutions for women: Getting the most of existing technologies today." Female condoms were highlighted in this panel about scaling up access to proven successful interventions. Learn more about the sessions (www.womendeliver.org/conferences/-2010-conference/agenda/plenary-sessions-indetail), view the video archives (www.womendeliver.org/conferences/-2010-conference/webcast), and find other information at the conference website (www.womendeliver.org/conferences).

Research on the FemCap as a Microbicide Delivery Device Presented at EBCOG 2010

Dr. Alfred Shihata presented new research on the FemCap at the European Board & College of Obstetrics and Gynaecology (EBCOG) Conference in Antwerp, Belgium, May 5-18, 2010. The FemCap is a cervical cap available for contraception in Europe and the United States and it also has potential as a microbicide delivery device for HIV/STI prevention (see the CBAS website for more information on the FemCap: www.cervicalbarriers.org/products/cervicalcaps.cfm). Dr. Shihita's research, entitled "Preventing pregnancy and sexually transmitted disease infections, by novel and

unique approach," demonstrated that the FemCap can be used to deliver a microbicide to the vagina while protecting the cervix from the microbicide by using Gentian dye to monitor where the microbicide went. More information about his research is available from Dr. Shihata's poster (www.cervicalbarriers.org/documents/Prevention_of_pregnancy_and_STI.pdf) and his PowerPoint presentation (www.cervicalbarriers.org/documents/ Revention_of_Pregnancy_and_STI_by_the_FemCap.ppt).

Microbicides 2010

The 2010 International Microbicides Conference was held in Pittsburg, Pennsylvania, May 22-25, 2010. The theme of the meeting was "Microbicides: Building bridges in HIV prevention" through collaborations between basic, behavioral, and clinical scientists, community partners, and advocacy groups. Please see below a list of posters and presentations that highlighted cervical barrier methods and visit the conference website for more information: www.microbicides2010.org.

- The Duet[®] cervical barrier used continuously or pre-coitally for HIV prevention in Zimbabwean women: An acceptability and safety study (Elizabeth Montgomery et al.)
- Vaginal practices, gel and barrier methods use among HIV prevention trial participants in southern Africa (Ariane van der Straten et al.)
- Development of microbicide-releasing SILCS diaphragm (Ian Major et al.) •
- Combining HIV prevention and contraceptive technologies (Gustavo Doncel et al.)
- Impact of learning HIV status on contraceptive use in the MIRA trial (Kelly Blanchard et al.) •
- Preference between precoital and continuous use of Duet[®] in Zimbabwe (Ariane van der Straten et al.)

(To view some of these posters and presentations, please visit the CBAS website.)





AICROBICIDES Building Bridges in HIV Prevention

Upcoming Events

Event: AIDS 2010 Date: July 18 – 23, 2010 Location: Vienna, Austria Website: www.aids2010.org/

Description: The 18th International AIDS Conference coincides with the 2010 deadline for universal access set by world leaders propelling a major push for expanded access to HIV prevention, treatment, care, and support. The theme, "Right here, right now" highlights the importance of human rights, which is a fundamental prerequisite to an effective response to the epidemic. Broader development and health goals will also be emphasized by considering the many opportunities for synergy and powerful alliances between these movements.

Event: Reproductive Health 2010 Date: September 22 – 25, 2010 Location: Atlanta, GA, USA Website: www.arhp.org/professional-education/ annual-meetings/rh2010

Description: This is the sixth joint annual meeting of the Association of Reproductive Health

Professionals, the Planned Parenthood Federation of America National Medical Committee, and the Society of Family Planning.

Event: American Public Health Association 2010 Annual Meeting and Expo Date: November 6 – 10, 2010 Location: Denver, CO, USA Website: www.apha.org/meetings/ Description: The 138th Annual Meeting & Exposition unites the public health community and offers them the opportunity to enhance their knowledge and share information on best practices and new trends in public health. The theme this year is "Social justice," which lies at the heart of public health. Sessions will explore why certain populations bear a disproportionate burden of disease and mortality and what the public health community can do to better address the causes of these inequities. There will be more than 1,000 cutting-edge scientific sessions and 700 booths of information and state-of-the-art public health products and services.

CBAS Steering Committee

Mags Beksinka: Maternal, Adolescent and Child Health, Department of Obstetrics and Gynecology, University of the Witwatersrand (MatCH) Marianne Callahan: CONRAD Tsungai Chipato: University of Zimbabwe-University of California, San Francisco Collaborative Research Programme in Women's Health Patricia Coffey: PATH Bidia Deperthes: United Nations Population Fund Maggie Kilbourne-Brook: PATH Helen Rees: Reproductive Health & HIV Research Unit of the University of the Witwatersrand, South Africa Kelley Ryan: Duke Clinical Research Institute Jill Schwartz: CONRAD Ariane van der Straten: Women's Global Health Imperative, RTI

Contribute to the CBAS Newsletter

To comment on anything you read in the CBAS newsletter or to contribute a story, event, or news item, please email info@cervicalbarriers.org.

About CBAS

What are cervical barriers?

Most people think of cervical barriers primarily as the diaphragm and cervical cap, but a broader definition would encompass Lea's shield, female and male condoms, the sponge, and microbicides. For more information about the range of cervical barrier methods, go to http://www.cervicalbarriers.org/information/methods.cfm.

Mission of CBAS (Updated!)

The Cervical Barrier Advancement Society (CBAS) aims to raise the profile of cervical barrier methods, including diaphragms, caps, female condoms, and other devices, for pregnancy prevention and to provide information about research on female condoms and the potential of cervical barriers to prevent sexually transmitted infections, including HIV.

Membership

CBAS membership is free and open to all who are interested in joining. CBAS's goal is to create an international, professional networking organization including clinical and social science research groups, academic institutions, advocacy groups, trade associations, and pharmaceutical, biotech, and medical device companies. As a member, you will have the opportunity to network and collaborate with other professionals in the field; keep abreast of new research; share information and ideas; and receive three newsletters per year.

CBAS Contact Information: For more information, contact Kelsey Otis, CBAS Executive Director, at kotis@cervicalbarriers.org. CBAS is coordinated by Ibis Reproductive Health (www.ibisreproductivehealth.org).