SILCS diaphragm: summary of clinical evaluations

WOMEN AS CO-DESIGNERS

The SILCS diaphragm is a single-size contraceptive barrier designed to fit a broad range of women. PATH led a user-centered design process across multiple sites and countries involving input from women, their partners, and providers. This feedback resulted in an innovative design that is easy and comfortable to use. PATH developed SILCS to expand women's options for nonhormonal protection.

The SILCS design features, like the contoured shape and patented spring technology, allow for one size of diaphragm to fit most women and overcomes issues that have limited broad use of earlier diaphragms. This means the product could be provided over the counter, and with minimal clinical support where allowed by regulatory approval and service delivery guidelines. This is especially important since provider time and resources in developing countries are limited.

NEED FOR NONHORMONAL METHODS

During recent decades, family planning programs have focused on hormonal contraception and intrauterine devices (IUDs). Awareness and promotion of diaphragms has dwindled. However, recent analysis of unmet need for family planning highlights the need for greater access to nonhormonal and user-initiated methods. Many women who do not want to become pregnant do not use a method due to concern about side effects, because they want a method that can be used intermittently, and/or can be used while breastfeeding. A diaphragm could meet the needs of some of these women.

In 2010, PATH licensed the SILCS technology to Kessel medintim GmbH for manufacturing and commercialization. The SILCS diaphragm achieved regulatory approval in 2013 and has been launched in more than 20 countries under the brand name Caya® contoured diaphragm. The United States Food and Drug Administration granted market clearance to the Caya® contoured diaphragm in late 2014 and in June 2015, Kessel launched the Caya® diaphragm in the United States.

Photo: PATH/Patrick McKern.

CLINICALLY PROVEN SAFETY, ACCEPTABILITY, AND COMFORT

Between 1998 and 2014, SILCS has been evaluated in ten studies in multiple countries. These include design validation and consumer use studies, as well as clinical studies of safety, effectiveness, and acceptability. SILCS has achieved high marks for acceptability, ease of use, and comfort among women and men—including even women with no previous diaphragm experience. The Phase II/III contraceptive effectiveness study found that SILCS used with a contraceptive gel has similar effectiveness to the Ortho All-Flex® diaphragm used with contraceptive gel.

Although SILCS was developed as a contraceptive method, it is also being evaluated as a reusable delivery system for microbicides. If these studies show that SILCS is a safe and effective way to deliver microbicides, this would allow SILCS to protect both from unintended pregnancy and HIV/sexually transmitted infections (STIs).

This document provides summaries of the key studies implemented during development and validation of SILCS as a barrier contraceptive. It also outlines current studies evaluating SILCS as a microbicide delivery system.

COMPLETED CLINICAL STUDIES

Preliminary assessment of fit and acceptability of Prototype V (1998)

Description	Sample	Product Uses	Endpoints	Key Findings
Fit and consumer acceptability of Prototype V (pre-Phase I).	18 couples	76	Fit and function during use. Safety and acceptability.	Results from this evaluation suggested that the SILCS diaphragm was easy, safe, and comfortable to insert, use, and remove.

CONRAD. *Preliminary Assessment of a New Silicone Barrier Contraceptive Device. Final Report.* 1998. [unpublished]

Phase I postcoital comparison of SILCS and Ortho All-Flex® diaphragms used with nonoxynol-9 (N-9) (2002)

Description	Sample	Product Uses	Endpoints	Key Findings
Phase I randomized, crossover comparison of SILCS/N-9 with Ortho All-Flex® diaphragm/N-9.	18 women	Ortho All-Flex® diaphragms: 17. SILCS diaphragms: 18.	Barrier effectiveness assessing motile sperm. Safety and acceptability.	Both the SILCS and the Ortho All-Flex® diaphragms performed well, reducing the average number of progressively motile sperm per high-powered field (HPF) to zero in the case of the Ortho All-Flex® diaphragm and to 0.1 for the SILCS diaphragm. No product-related adverse events were reported. Women who had used a diaphragm before reported the SILCS diaphragm was much better in terms of insertion and comfort than other diaphragms.

CONRAD. *A Phase I Comparative Postcoital Testing and Safety Study of the SILCS Diaphragm vs. the Ortho All-Flex® Diaphragm.* 2002. [unpublished]

Magnetic resonance imaging (MRI) of SILCS diaphragm: anatomical considerations and corroboration with clinical fit (2007)

Description	Sample	Product Uses	Endpoints	Key Findings
Pilot study to assess *in vivo* fit of SILCS diaphragm among women of varying body mass and parity. MRI scans taken at baseline, after SILCS insertion, and after simulated coitus.	Six pre-menopausal women representing different body mass index (BMI) categories.	24	Fit of SILCS diaphragm *in vivo* in a cross-section of women.	SILCS diaphragm was easily identified on MRI. In all subjects, the diaphragm covered the cervix. The position of the diaphragm did not change after simulated intercourse. MRI confirms the anatomic position of the SILCS diaphragm *in vivo*, among a sample of women varying in body mass and parity.

Yang CC, Maravilla KR, Kilbourne-Brook M, Austin G. Magnetic resonance imaging of SILCS diaphragm: anatomical considerations and corroboration with clinical fit. *Contraception.* 2007;76(3):238–244.

Phase I postcoital testing (PCT) of a single-size SILCS diaphragm used with N-9 (2008)

Description	Sample	Product Uses	Endpoints	Key Findings
Crossover PCT study in sexually active women. Couples compared use of SILCS (metal spring) + N-9 to SILCS + K-Y® Jelly. A subgroup of couples also used the SILCS polymer spring device + N-9.	12 couples completed main study, (SILCS metal spring). Eight couples completed sub-study (polymer spring).	20	Barrier performance of SILCS used with either N-9 or lubricant in preventing sperm from penetrating mid-cycle cervical mucus. Safety and acceptability.	SILCS diaphragm (metal and polymer spring) used with N-9 reduced the number of progressively motile sperm per HPF from a baseline of 12.5 to zero. With K-Y® Jelly, the SILCS diaphragm reduced the number of sperm per HPF to 0.5. No adverse events associated with product use. The polymer spring device improved fit in the subset of women who failed screening due to fit problems with the metal spring device.

Schwartz JL, Ballagh SA, Creinin MD, Rountree RW, Kilbourne-Brook M, Mauck CK, Callahan MM. SILCS diaphragm: postcoital testing of a new single-size contraceptive device. *Contraception.* 2008;78(3):237–244.

Short-term acceptability of a single-size diaphragm among couples in South Africa and Thailand (2008)

Description	Sample	Product Uses	Endpoints	Key Findings
Non-randomized, non-blinded, non-significant risk study to assess acceptability among women with no previous diaphragm experience.	41women	164	Function, safety, and acceptability.	The SILCS diaphragm fits women representing a range of diaphragm sizes (65–80 mm), parity (0–4); and BMI normal to obese. Women and men, including those with no previous experience with diaphragms, reported that the SILCS diaphragm was acceptable and easy to use.

Coffey PS, Kilbourne-Brook M, Beksinska M, Thongkrajai E. Short-term acceptability of a single-size diaphragm among couples in South Africa and Thailand. *Journal of Family Planning and Reproductive Health Care.* 2008;34(4):233–236.

Comparative acceptability of SILCS and Ortho All-Flex® diaphragms among couples in the Dominican Republic (2008)

Description	Sample	Product Uses	Endpoints	Key Findings
Randomized, crossover comparison of SILCS diaphragm to Ortho All-Flex® diaphragm, used with K-Y® Jelly.	20 couples	160 product uses: (80 for SILCS; 80 for Ortho All-Flex® diaphragm).	Fit and function during use. Safety and acceptability.	SILCS diaphragm fit women representing diaphragm sizes 70–85 mm; parity (0–7); and BMI (normal to obese). Women and men, including those with no previous experience with diaphragms, reported that the SILCS diaphragm was acceptable and easy to use. High acceptability for insertion, removal, comfort, and sensation. Good sensation and comfort for male partners. The SILCS device was preferred over the Ortho All-Flex® diaphragm by both female and male participants.

Coffey PS, Kilbourne-Brook M, Brache V, Cochón L. Comparative acceptability of the SILCS and Ortho All-Flex® diaphragms among couples in the Dominican Republic. *Contraception*. 2008;78(5):418–423.

Acceptability of three cervical barriers among vulnerable young women in Zimbabwe (2010)

Description	Sample	Product Uses	Endpoints	Key Findings
Mixed-methods exploratory study included focus group discussions (FGDs) and clinical use. Women (aged 16–21) were invited to practice inserting/removing one of three randomly assigned cervical barriers (Ortho All-Flex®; FemCap; SILCS diaphragm).	45 young women.	45	Feasibility and acceptability of contraceptive barrier use among young women. Preferences and attitudes toward use. Attitudes about use for dual protection.	All 45 women were able to insert their assigned device. The majority reported "easy" insertion and removal, and 93% liked the device they tried. When asked which device they would like to try in the future, over half (58%) chose SILCS regardless of which device they had tried. The majority felt comfortable touching their genitals to insert/remove the barrier device. Fewer than 7% of participants had concerns about privacy or storage, or learning how to use a contraceptive barrier device.

Van der Straten A, Sahin-Hodoglugil N, Clouse K, Mtetwa S, Chirenje MZ. Feasibility and potential acceptability of three cervical barriers among vulnerable young women in Zimbabwe. *Journal of Family Planning and Reproductive Health Care*. 2010;36(1):13–19.

Phase II/III pivotal contraceptive effectiveness study (2010)*

Description	Sample	Product Uses	Endpoints	Key Findings
Multi-center trial contraceptive effectiveness study. 300 women used SILCS + BufferGel® (BG). 150 women used SILCS + N-9 spermicide. Effectiveness and safety results were compared to an historical control group who used the Ortho All-Flex® diaphragm with these gels. No statistical comparison between gels (BG and N-9) was planned.	450 women.	SILCS used as primary contraceptive method for six months. Minimum four sex acts per month.	Pregnancy probability, safety, acceptability, fit, and ease of use.	SILCS was safe, effective, and acceptable when used with a contraceptive gel. A total of 421/450 women (94%) provided follow-up data. There were 35 study pregnancies yielding a six-month Kaplan-Meier cumulative typical-use pregnancy probability of 10.4 per 100 women [95% confidence interval (CI) (6.9, 14.0)] overall, 9.6 (5.5, 13.6) for SILCS with BG and 12.5 (5.4, 19.5) for SILCS with N-9. 98% of women could be fit with the SILCS; 82% said they liked the SILCS. An historical control analysis concluded that the SILCS diaphragm was non-inferior to the Ortho All-Flex® diaphragm.

Schwartz JL, Weiner DH, Lai JJ, et al. Contraceptive efficacy, safety, fit, and acceptability of SILCS, a single-size diaphragm developed with end-user input. *Obstetrics and Gynecology*. 2015;125(4):895-903.

STUDIES OF SILCS FOR MICROBICIDE GEL DELIVERY

MRI study of microbicide delivery with SILCS diaphragm compared to a vaginal applicator (2010)

Description	Sample	Product Uses	Endpoints	Key Findings
Exploratory, randomized crossover study among women aged 18–45 years. MRI assessed gel distribution/retention when BG was delivered via SILCS (single-sided or double-sided application) and a vaginal applicator.	Six women. (Three completed all study procedures.)	SILCS single-sided (5 ml). SILCS double-sided (2.5 ml in cervical cup; 2.5 ml in vagina). Vaginal applicator (5 ml) only.	Gel distribution and retention in the upper and lower vagina assessed by MRI: immediately after gel insertion, immediately after simulated intercourse, and six hours after simulated intercourse.	MRI analysis indicated similar gel spread in the vagina among all three methods. SILCS single-sided gel application resulted in the most consistent longitudinal coverage. SILCS double-sided gel application was most consistent in transverse dimension. These results suggest that SILCS is comparable to vaginal applicators for intravaginal microbicide gel delivery.

Pentlicky S, Rosen M, Coffey PS, Kilbourne-Brook M, et al. An exploratory, randomized, crossover MRI study of microbicide delivery with the SILCS diaphragm compared to a vaginal applicator. *Contraception.* 87(2013):187–192.

Couples' acceptability of SILCs diaphragm for microbicide delivery (2009)

Description	Sample	Product Uses	Endpoints	Key Findings
Randomized, crossover study comparing single- and double-sided SILCS gel delivery to gel delivered from an applicator. Women, aged 18–45 years, sexually active in a monogamous relationship, and using a non-barrier method of contraception were eligible. BG was the investigational gel used in this study.	36 couples. (34 couples completed the study.)	204 Each couple used each gel delivery scenario during two sex acts.	Ease of application. Acceptability. Perceived effectiveness for pregnancy and disease prevention. Overall preference. Willingness to purchase.	All three scenarios received favorable ratings for ease of application, acceptability, and perceived effectiveness. Both female and male participants rated the applicator more favorably than SILCS for all attributes except messiness/leakage and effectiveness. Further research of SILCs as a microbicide delivery system should assess acceptability among study populations that reflect diverse potential user groups (women and men from both low- and high-HIV-prevalence settings, and populations with and without experience using female barrier methods).

Frezieres RG, Walsh T, Kilbourne-Brook M, Coffey PS. Couples' acceptability of the SILCS diaphragm for microbicide delivery. *Contraception.* 85(2013):99–107.

CLINICAL STUDIES IN PROCESS

Study	Recruitment Sample	Purpose
Phase I parallel double-blinded safety and acceptability study of SILCS + Contragel (2014–2015).	50	Evaluate the systemic and genitourinary safety of Contragel used with a SILCS diaphragm compared to HEC placebo used with SILCS diaphragm during two seven-day periods of daily use (without and with intercourse).
Phase I randomized, crossover comparative PCT study of SILCS + Contragel (2014–2016).	40	Compare barrier effectiveness via PCT of SILCS used with Contragel compared to SILCS used with N-9, and SILCS used with no gel.
Pre-Phase I. Randomized comparative study in Durban, South Africa among women aged 18-45 years, and a subset of male partners.	115 Mixed methods, including clinical use and FGDs.	Assess acceptability and preferences of SILCS diaphragm for gel delivery compared to prefilled vaginal applicators for gel delivery and using dosing according to the BAT24 regimen used for microbicide gel delivery.

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PATH developed the SILCS diaphragm with partners including CONRAD and researchers in multiple countries. In 2010, the technology was licensed to Kessel medintim GmbH for commercialization.

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PRODUCT INQUIRIES

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