Reinventing the Past to Reshape the Future of Contraception

THE STORY OF THE SILCS DIAPHRAGM

This demonstrates the best of what multisector collaboration can achieve when we harness our shared expertise to develop solutions that can improve the health of women and their families around the world.

– Steve Davis, PATH President and CEO

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Photos: (cover) PATH/Patrick McKern, (above) PATH/Maggie Kilbourne-Brook

Women said they wanted access to more methods that were under their control, had no side effects, and could protect from STIs. We thought that sounds a lot like a diaphragm, so we asked why had diaphragms stopped being available?

– Maggie Kilbourne-Brook, Senior Program Officer, PATH

Improved access to family planning is one of the world's greatest international development success stories over the last 40 years. Still, 225 million women in developing regions around the globe face an unmet need for contraception. For women who cannot or do not want to use hormonal methods or an intrauterine device (IUD), or whose partner will not use condoms, options are few. They face increased infections, unwanted pregnancies, and little control over their reproductive health.

Today, SILCS—a contoured diaphragm that a woman can use to take control of her reproductive health—is available to meet these women's needs. For 20 years, PATH and its partners worked together to develop, validate, manufacture, introduce, and scale the world's first new diaphragm in 50 years to reach the market. Currently marketed by Kessel medintim GmbH as the Caya® contoured diaphragm, SILCS is now providing greater reproductive health freedom to women in more than 25 countries.

This is the story of how SILCS was inspired and shaped by women and couples around the world to be comfortable, simple to use, and easy to provide. It is the story of how a wide range of partners collaborated with PATH to bring the product to life—from early design development partner SILCS, Inc., to German manufacturer Kessel medintim GmbH (Kessel), to funder the United States Agency for International Development (USAID), research and regulatory partner CONRAD, and researchers across the globe.

Today the SILCS story continues to unfold. After successful introduction in developed and middle-income countries, the diaphragm is now poised to reach markets in low-income countries where women need it most. Studies are building evidence for its potential as a multipurpose prevention technology (MPT) that could act as a delivery system for microbicide gel or antiretroviral (ARV) drugs for HIV prevention. A new and exciting future lies ahead as Kessel works with country-level partners, providers, and advocates to expand access to the Caya diaphragm to meet the needs of women who are seeking an option for nonhormonal contraception.

Photo: PATH/Glenn Austin

® Caya is a registered trademark of Kessel medintim GmbH

The Birth of SILCS

In 1994, in preparation for the International Conference on Population and Development, researchers met with women from diverse regions around the world to understand their experience with contraceptives. They asked women what they liked or disliked about their current family planning options and what they would like in a contraceptive method in the future. Women stated clearly that they wanted a method that was under their control and had few side effects.

Traditional diaphragms: benefits and challenges

The diaphragm is a barrier device that a woman inserts into her vagina before sex to block sperm from entering the cervix. About six hours after sex, she removes the diaphragm and washes and stores it in its case until next use. Diaphragms are recommended for use with a contraceptive gel, which is inserted into the cervical cup before use. Diaphragms are reusable for two years or longer.

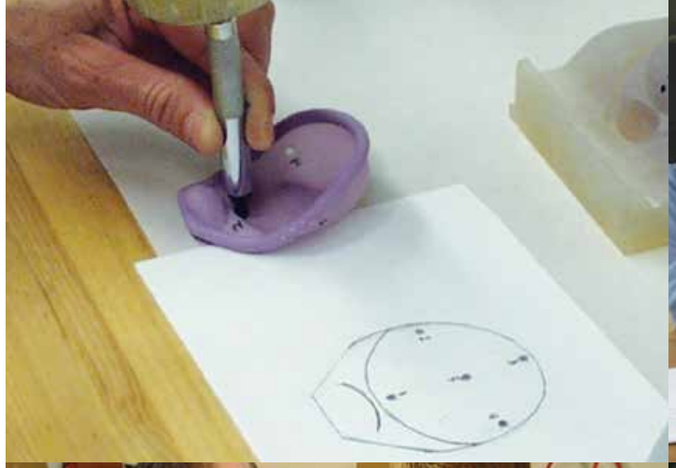
Widely used in past decades, diaphragms stopped being promoted over time as providers opted for more modern and highly effective methods such as oral contraceptive pills, IUDs, and injectable contraceptives. Traditional diaphragms can be difficult to supply and provide—especially in resource-constrained settings—because they come in multiple sizes and require a pelvic exam and trained provider to determine which size a woman can wear. Some women find the traditional diaphragm difficult to handle and insert and uncomfortable to wear for the recommended six hours after sex.

At the PATH product development shop in Seattle, Washington USA, a small team of public health researchers and product developers realized that what these women wanted sounded a lot like a diaphragm. At the time, though, diaphragms were hardly promoted or available in family planning programs. Traditional diaphragms had features that made them difficult to supply, provide, and use—especially in resource-limited settings. As a result, providers had switched to promoting other methods, like hormonal contraception and IUDs, and diaphragm use had declined.

Still, the PATH team thought they could create a new, innovative diaphragm that could overcome these challenges. They knew that a nonhormonal, user-initiated product that was appropriate for use in low-resource settings could help address a significant gap in the contraceptive method mix. Their experience employing user-centered design processes for health technology solutions—coupled with advances in manufacturing, materials, and knowledge of vaginal anatomy—gave PATH the confidence to move forward to reimagine the diaphragm. At the same time, PATH's vision coincided with the interests of CONRAD (a Division of the Department of Obstetrics and Gynecology at the Eastern Virginia Medical School), which could offer research and clinical support, and USAID, which provided valuable funding for the project. Both CONRAD and USAID agreed with PATH that a redesigned diaphragm could meet the needs of the many women not being served by current contraceptive options.

Until SILCS, most diaphragms were round, with a stiff spring, and designed for a "wedged" fit in the vagina. This design was developed around ease of manufacturing, not with women's anatomy in mind. This design has hardly changed in more than 100 years.

Photo: Cervical Barrier Advancement Society



PATH and its partners developed the SILCS diaphragm—through a user-centered development process involving input from women, their partners, and providers—to expand women's options for nonhormonal barrier contraception.

Photos: PATH

Not Your (Grand)mother's Diaphragm

DEVELOPING THE PRODUCT (1994–2004)

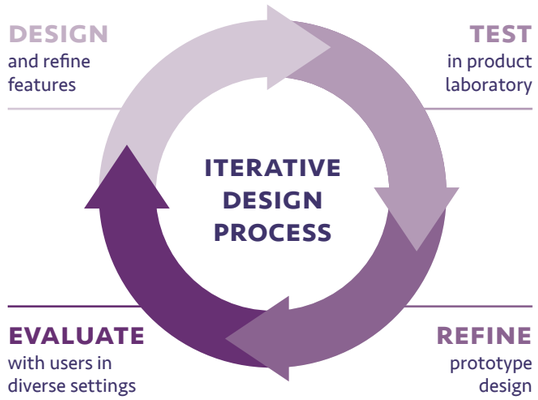
"Product development is an iterative process. Using input from women and providers, we developed successive prototype designs that were tested and refined to meet user-based product performance criteria. Each feature and combination of features was evaluated to ensure an improvement in one did not result in an unexpected negative with another. The result is a design that is easy to use—especially for new users."

– Glenn Austin, Senior Technical Officer, PATH

With funding from USAID through CONRAD, a product development team at PATH embarked on feasibility research to understand how to make a diaphragm that would be easy to supply, provide, and use. The PATH team realized their success would hinge on gathering and incorporating input from users and other stakeholders. They surveyed women to learn from their experiences using diaphragms—what they liked and did not like, and what could be improved. The team also gathered input from family planning providers and donors to learn about other barriers and obstacles to providing diaphragms. Research and evaluations began in Seattle, branched out to multiple sites in the United States, then took place in the Dominican Republic, South Africa, Thailand, and finally Zimbabwe.

PATH's user-centered design process identified the performance criteria that a new product would need to achieve. This became the roadmap for development. Women said they wanted a diaphragm that was easy to handle and insert, comfortable to wear—especially for six hours—and would be comfortable for both partners during sex. Donors and procurement groups wanted a diaphragm that would be easy to order and supply and that did not require multiple sizes. Family planning providers wanted a diaphragm that would be easy for a new user to learn to use and would not require a fitting exam.

Prototype designs were first fabricated by hand-cast silicone in the PATH product development laboratory in Seattle. These early prototypes were evaluated in bench tests, and eventually by women and providers in clinics. Features such as material thickness, shape, and spring design were refined in response to their feedback. Once there was confidence in the feature set, fabrication shifted to machine manufacturing using an injection molding process at SILCS, Inc., the early manufacturing partner. Silicone injection molding allowed the design to be very thin and flexible but required finesse in manufacturing. The manufactured prototypes were evaluated by larger groups of women at clinics, and eventually in couples' use studies. Again, women and providers gave feedback about ease of handling, insertion, and removal, as well as comfort. After each round of evaluation, features were refined to address fit, functionality, and comfort, and then the next design iteration moved through the process. During the design phase, PATH tested nearly 200 variations of features before settling on the right combination.



The result was the SILCS diaphragm, with user-friendly features that make it easy to use and comfortable to wear. "Grip dimples" provide a cue for the user about where to squeeze the diaphragm during insertion, and a finger dome helps with removal. The contoured spring design allows this single-size device to fit a broad range of women. A final-stage refinement replaced a three-piece metal spring with a nylon spring. This change—designed to improve manufacturability—reduced cost and improved comfort and fit in a broader range of women.

"The SILCS diaphragm, a contoured single-size silicone device, is comfortable, easy to use, and does not require a pelvic examination for fitting, a major disadvantage in low-resource settings."

– Dr. Lindsay Edouard, United Nations Population Fund (2012)

The SILCS diaphragm

PATH translated what they heard from women and other stakeholders into the design and performance objectives that a new device must achieve to overcome the obstacles of traditional diaphragms:

- **Easy to supply and provide—single size, with no pelvic exam required**
- **Easy to insert—especially for new users**
- **Comfortable for both partners**
- **Easy to remove**
- **Durable under harsh conditions**

Early versions of the SILCS diaphragm prototypes. Design elements such as grip dimples, removal features, spring shape, and cervical cup evolved based on user/provider feedback.

Photos: PATH

Building Evidence

CLINICAL STUDIES (1998–2014)*

> “In the recent contraceptive effectiveness study, 76 percent of women were able to insert and correctly position the diaphragm simply using instructions. With coaching, 94 percent of women were able to insert, correctly position, and remove the diaphragm.”
>
> – Gustavo Doncel, MD, PhD, Scientific and Executive Director of CONRAD (2015)

Once the PATH team had a design that was easy to handle, insert, and wear, they and their partners began testing it in clinical studies at multiple sites and among potential users in low-resource settings. The team had to ensure that their single-size device really could fit most women, was acceptable to couples in diverse settings and cultures, and was easy to use—especially for new users. Then the diaphragm needed to be evaluated for how it performed when women used it for contraception.

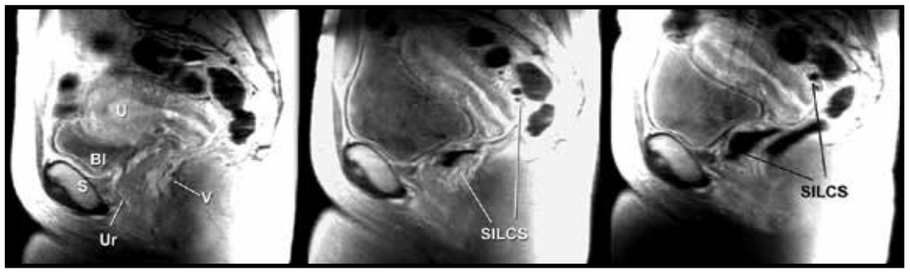
Between 1998 and 2014, PATH, CONRAD, and other partners generated evidence about the SILCS diaphragm through ten studies in multiple countries. SILCS achieved high marks for acceptability, safety, barrier effectiveness, and ease of use among couples in developed and developing countries, including those with no previous diaphragm experience.

Clinical validation (1998–2004)

CONRAD implemented three clinical studies to validate safety, acceptability, and barrier effectiveness of the new diaphragm. First, a couples’ use study in the United States confirmed the SILCS diaphragm was easy to use and comfortable during sex.

Next, CONRAD implemented a Phase I study to evaluate SILCS safety, acceptability, and barrier effectiveness. This postcoital study tested how well the SILCS diaphragm blocked sperm from entering the cervix when the diaphragm was used with a contraceptive gel during sex. When CONRAD compared the SILCS diaphragm results to the traditional diaphragm that comes in multiple sizes, they found that SILCS barrier effectiveness was good. However, some women had difficulty obtaining a good fit with SILCS.

Once refinements were made to the cervical cup and spring, based on women’s and providers’ feedback, CONRAD implemented a second postcoital study, which found the refined SILCS diaphragm addressed the fit issues identified in the previous study, performed “as well as” the traditional diaphragm in blocking sperm, and was preferred by women for its ease of use and comfort.



PATH and the University of Washington used magnetic resonance imaging to “see” how SILCS fits in the vagina and covers the cervix.

Photo: University of Washington/CC Yang and KR Maravilla

* As of 2016, the SILCS diaphragm has been evaluated in 14 clinical studies in five countries to build evidence of its safety, acceptability, and ease of use, and effectiveness. A summary of clinical studies is available at http://www.path.org/publications/files/TS_silcs_diaphragm_clinical_eval_fs_june.pdf.

At the same time, the PATH team worked with researchers at the University of Washington (UW) to build evidence that the single-size SILCS fit women representing a range of diaphragm sizes. UW researchers implemented a magnetic resonance imaging (MRI) study to “visualize” the fit and position of the SILCS in a variety of women. MRI scans showed that the SILCS device fit well in women representing underweight, normal, and obese body mass index (BMI). These data, along with fit results from clinical studies showing that SILCS fits women who wear the most common diaphragm sizes (65 to 80 mm), would become part of the United States Food and Drug Administration (USFDA) regulatory filing.

Couples’ use studies in low-resource settings (2002–2004)

After the CONRAD couples’ use study confirmed performance and safety of the device, PATH collaborated with researchers in the Dominican Republic, South Africa, and Thailand to assess fit, ease of use, and acceptability with couples in these diverse regions. PATH partnered with researchers who were interested in learning about user-centered research and were trusted in their communities to implement sensitive research on sexual topics.

Both women and their partners provided feedback on using the SILCS diaphragm to understand how it affected satisfaction and comfort during sex. The studies confirmed that the single-size diaphragm fit women from diverse geographic regions, with a wider range of BMI and parity than was found in the US study population. Women with no previous experience

> “It feels like it belongs to you. Sometimes you think, ‘do I have it on or not?’”
>
> – Female, Dominican Republic

> “I like it better than sex without the diaphragm. My partner was quite satisfied...”
>
> – Male, Dominican Republic

Couples’ use study results from three countries*

N=63 couples

Easy to handle and insert:	**85%**
Stable during use:	**97%**
Comfortable for both partners during use:	**>95%**
Good sensation for both partners:	**>95%**

*SILCS Acceptability in Three Countries. Presented at: International Microbicides Conference, April 23–26, 2006; Cape Town, South Africa.

SILCS achieved high marks for acceptability, safety, barrier effectiveness, and ease of use among couples in developed and developing countries, including those with no previous diaphragm experience.

Photo: iStock

Typical and perfect use pregnancy probabilities* for SILCS plus contraceptive gel at 6 months and extrapolated to 12 months

	6 MOS.	12 MOS. (extrapolated)
TYPICAL USE	10.4	17.8
PERFECT USE	7.9	13.7

* Estimated number of pregnancies per 100 women during time period.

Adapted from Schwartz JL, Weiner DH, Lai JJ, et al. 2015. doi: 10.1097/AOG.0000000000000721.

> "I reach orgasm better than usual. I feel excited every time I use it. I think it is very economical and can be used many times."
>
> – Female, Thailand

> "You feel like you are safe when using this kind of device unlike male condoms."
>
> – Female, South Africa

> "...[the diaphragm is] available when needed unlike male condoms, which sometimes run out and you end up having sex without."
>
> – Male, South Africa

easily learned to insert and use the diaphragm. SILCS was acceptable to women and their partners. Washing and reusing the diaphragm was not bothersome or problematic—even women in low-resource settings found strategies to manage this. Some couples in South Africa specifically liked that the diaphragm is reusable, since this will be more cost-effective. In the Dominican Republic, some men reported liking the sensation of sex more when their wife used the diaphragm than sex without the diaphragm.

Contraceptive effectiveness: The critical evaluation for regulatory approval (2008–2010)

Before SILCS could receive regulatory approval and enter the market, a contraceptive effectiveness study was needed to test how the SILCS diaphragm worked when women relied on it to prevent pregnancy. Up until this time, SILCS study participants had been protected from pregnancy by using another family planning method, since those studies were designed to assess ease of use and acceptability.

After discussions with the USFDA and researchers regarding study design, and overcoming the challenge when the contraceptive gel intended for this study became no longer available, CONRAD implemented a contraceptive effectiveness study among 450 women across six sites in the United States. These women used the SILCS diaphragm plus a contraceptive gel as their primary contraceptive method for six months. Data from this study confirmed good fit and safety and determined that SILCS provided protection similar (i.e., "noninferior") to a traditional diaphragm when both were used with a contraceptive gel. This study also confirmed that women could learn to insert and check fit using the written and pictorial instructions alone. With this, the last pieces of clinical evidence required to support regulatory submissions for market access fell into place.

CONRAD—the clinical and regulatory sponsor of the SILCS diaphragm—implemented multiple studies, including the contraceptive effectiveness study and safety and barrier effectiveness studies of Contragel.
Photo: CONRAD

Readying for Launch

MANUFACTURING, PACKAGING, REGULATORY APPROVALS (2010–2013)

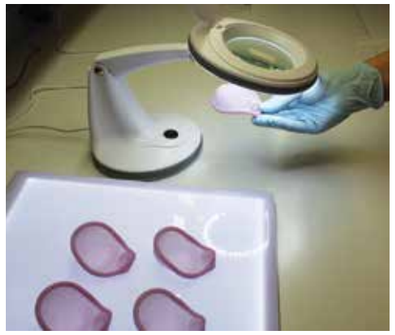
> "USAID has supported the SILCS Diaphragm from the early days of its development. We see new technologies, like the SILCS Diaphragm, as essential to meet global family planning goals, including reaching 120 million more women and girls with family planning information and services by 2020."
>
> – Ellen Starbird, Director of USAID's Office of Population and Reproductive Health (2014)

Now it was time for PATH to focus on the next critical step toward market access: identifying a commercialization partner that had the capacity and expertise to bring this technology from clinical validation to manufacturing and marketing. To bring the product to market, they chose Kessel medintim GmbH, a German family-run company, headed by CEO Martin Kessel, which manufactures and markets sexual health products to more than 40 countries through a network of partnerships. In 2010, Kessel already had experience in marketing diaphragms and cervical caps and believed the SILCS diaphragm would be a good addition to its portfolio. Partnering with Kessel allowed PATH to leverage the company's expertise in manufacturing, regulatory submissions, and marketing. Kessel also has global distribution rights to ContraGel, a lactic acid based contraceptive gel developed as an alternative to nonoxynol-9 gel.

Scaling up manufacturing

PATH and Kessel negotiated a licensing agreement whereby PATH transferred the SILCS technology to Kessel. In return, Kessel accepted the responsibility to manufacture and market the product through its existing channels and bring SILCS to low-resource settings with preferential pricing for the public sector in order to expand access. During 2010 through 2012, Kessel established and refined the manufacturing process to reduce costs and scaled manufacturing from the small-scale batches that had been sufficient for clinical studies to a manufacturing process ready for initial market launch.

By late 2012, production was validated with an optimized manufacturing process, which included using retractable pins to hold the contoured spring in the



Caya production and quality control at Kessel's manufacturing facility.
Photos: Kessel medintim GmbH

mold during the injection molding process. Over time, manufacturing improvements reduced the cost of SILCS from almost US $20 per unit at small production volumes of 500 units used for clinical trials to about $5 per unit (2013) per unit at production batches of 10,000 units. Through manufacture of additional batches in subsequent years, Kessel has continued to optimize manufacturing to reduce reject rate and increase yield. They apply this cost savings to building market access.

Preparing the product offering for market launch

In addition to manufacturing, Kessel developed a new brand for the single-size, contoured diaphragm. Although SILCS was the name used during product development and research studies, Kessel decided to use the brand Caya® contoured diaphragm for the commercial product. Instructions and provider materials—developed and evaluated through clinical studies—were refined for product launch. Kessel developed seven products to prepare for marketing, including a contoured storage case; outer packaging and labeling; a printed instruction booklet and an animated DVD of instructions, translated into five languages; a pelvic model for demonstration; a provider manual of technical information; and a marketing brochure. The company also rebranded its existing contraceptive gel, Contragel®—a lactic acid based contraceptive gel, CE Mark–approved for use with a diaphragm—as CayaGel® and amended the European dossier for this new package and name.

To make sure consumers could comprehend the key safety and user instructions on the packaging, one final study was conducted in 2011 by the California Family Health Council on the boardwalk in Venice Beach, California. Nearly 90 percent of participants, from various ethnic and educational backgrounds, correctly answered 17 or more of the 20 questions on the comprehension questionnaire and confirmed the key messages were understandable by most women.

® Contragel and CayaGel are registered trademarks of Kessel medintim GmbH

Researchers went to the boardwalk in Venice, CA to recruit a cross section of women for the label comprehension study.
Photo: California Family Health Council (CFHC)

Kessle developed an array of marketing materials to support Caya introduction, now available in 14 languages.
Photo: PATH/Patrick McKern

PATH team celebrating the CE Mark approval in April 2013.
Photo: PATH/Patrick McKern

Regulatory approvals and country registrations by Kessel and partners:	
Europe CE Mark	2013
Canada Health	2013
Australia TGA*	2013
Malaysia MDA**	2014
USFDA	2014
Malawi	2015
Zambia	2015
Morocco	2016
Israel	2016
Nigeria	Under way
Uganda	Under way

* Therapeutic Goods Admistration
** Medical Device Authority

Regulatory approval

Before any contraceptive device comes to market, regulatory approvals are required in the country where it will be introduced. While Caya was created to reach developing-country markets, PATH and Kessel agreed that regulatory approval—and subsequent introduction—in developed countries, including Europe and the United States, would help raise awareness for this new method and build market confidence. Experience in Europe and the United States could also help policymakers, researchers, and family planning providers in low-resource settings better evaluate introduction of Caya into their programs.

EUROPE

Because there was strong interest in Europe for the new diaphragm, Kessel and PATH focused first on gaining the European CE Mark. Entering European Union (EU) markets first allowed Kessel to gain experience with building supply and market demand in countries where Kessel has existing distribution networks. In Europe, Caya is approved for over-the-counter (OTC) provision, which means that in most EU countries women can buy the product without getting a prescription or visiting a provider. (France and Italy decided to provide it by prescription).

UNITED STATES

After the Caya contoured diaphragm launched in Europe in June 2013, Kessel and PATH turned toward compiling the regulatory dossier required by the USFDA. The European regulatory dossier, as well as additional analysis of data by CONRAD and FHI360 from the contraceptive effectiveness study, provided the foundation for USFDA regulatory submission, which was first submitted in February 2014. The USFDA completed its review of the Caya 510(k) submission, clearing Caya for marketing in the United States in September 2014.

Although Caya is approved for OTC provision in Europe, the USFDA indicated an additional study would be required to determine whether OTC would be safe for women in the United States, so the Kessel Caya regulatory submission did not request review as an OTC device.

While many stakeholders believed OTC would be a valuable strategy for improving access for women in the United States, market research suggested that women preferred obtaining the Caya diaphragm via a clinic—especially new diaphragm users—primarily due to lack of familiarity with the method. Kessel and PATH determined that their key objective was to gain USFDA approval of the Caya diaphragm so it could enter the market and build consumer experience. Based on consumer and provider experience with Caya as a prescription device, then Kessel could decide in the future whether there were sufficient interest to build the evidence required to request a change to OTC status. Successful marketing of Caya in Europe as an OTC device was sufficient precedent for OTC service-delivery scenarios in low-resource countries in the future.

> “FDA market approval comes rarely to product development teams and only after much blood, sweat, and tears by many. This is a great accomplishment for PATH and its partners—and most importantly for women in the United States and around the world.”
>
> – David Kaslow, Vice President of Product Development and head of the Center for Vaccine Innovation and Access, PATH

Introducing Caya

MARKET INTRODUCTION (2013)

> “It is vitally important to expand access in the United States to methods that expand women’s pregnancy and STI prevention options.”
>
> – Wayne C. Shields, President and CEO at the Association of Reproductive Health Professionals

After 36 months of preparation, Kessel announced the first Caya contoured diaphragm product launch in April 2013 in six European countries. Within a year, Caya had expanded to 14 countries, and within two years, Caya sales via Kessel and its partners reached 20 countries. As of 2016, Caya is available in more than 25 developed and middle-income countries, including the United States.

Consumer marketing surveys conducted annually in Germany by Kessel helped characterize these early adopters of the Caya diaphragm. In the 2016 survey, 57 percent of Caya users reported switching from hormonal methods, with most of these (45 percent) having switched from oral contraceptive pills. Interestingly, almost 10 percent of Caya users reported not having used any contraceptive method previously. These surveys indicate that Caya users represent a wide age range (from <18 years to 45+ years), and the number of young women choosing Caya increased from 14 percent (2014) to 37 percent (2016) of survey respondents when looking at <18 years and 18 to 25 years combined.

Kessel’s business philosophy—that women and providers have access to the information they need to use and provide the Caya diaphragm safely and appropriately—has been key to the success of Kessel’s marketing strategy. In Europe, Caya was introduced initially to family planning providers via conferences, meetings, and mailings. After several months of provider outreach, Kessel began limited outreach to consumers. Across the continent, word spread quickly through online resources and social media to a new generation of women looking for alternative contraceptive options. Online resources such as the Cervical Barrier Advancement Society—a resource for information about diaphragms, cervical caps, and female condoms—and a digital user group that provides information and support to women using or considering using diaphragms or cervical caps bolstered outreach.*

For its US marketing effort, Kessel partnered with HPSRx Enterprises, Inc., a wholesale distributor specializing in women’s health. After the 2015 launch, PATH and a network of reproductive health nongovernmental organizations (NGOs) helped publicize the availability of Caya through print, digital, radio, and social media coverage, including more than 25 articles, interviews, and blog posts. Within two weeks, PATH documented more than 125,000 page views or downloads for information about the SILCS/Caya diaphragm from its program website.

In 2015, Kessel launched a Caya Facebook page in Germany. In 2016, the Facebook page went “international,” spreading the word to new audiences, including those in countries where Caya is not yet available. Within the first month, for example, the Caya Facebook page received more than 12,000 “likes” from Nigeria, which bolstered the interest of the local social marketing group.

During this time, Kessel, PATH, and partners presented at regional and international meetings of organizations such as the European Society of Contraception and Reproductive Health and the International Conference on Family Planning, as well as the Microbicides, HIV Research for Prevention, and AIDS conferences, to raise awareness about this new barrier method among family planning and sexual and reproductive health stakeholders globally.

Kessel’s business-to-business model relies on a network of distributors who are known and respected in their communities. With the sharpened focus on the need to develop markets sustainably and the donor community’s desire to leverage private-sector expertise to build consumer markets, Kessel’s approach is proving successful in broadening Caya’s reach. Product launches in Europe and the United States generated awareness and interest among consumers and providers in other countries. Now work is under way to build partnerships for Caya introduction in low-income countries, such as India, Nigeria, and Uganda, where the need for Caya is greatest.

Country access from June 2013 to June 2016

2013 | Caya is launched in June to 6 EU countries
2014 | Caya is sold in **20 countries**
2015 | Caya is sold in **25 countries**
2016 | Caya is sold in **28 countries**

The Kessel team celebrating the first sale of Caya in Germany in 2013.
Photo: Kessel medintim GmbH

*DiaphragmsAndCaps discussion board (women members only). Available at: https://groups.yahoo.com/neo/groups/DiaphragmsAndCaps/info.

Martin Kessel introduces the Caya diaphragm to interested participants at the International Family Planning Conference in Nusa Dua, Indonesia, January 2016.
Photo: PATH/Maggie Kilbourne-Brook

Readying for Introduction in Low-resource Countries

(2010–2016)

> “The SILCS barrier method has the potential to avert health outcomes from unintended pregnancies, particularly for women in resource-poor settings, and will form part of the World Health Organization’s strong commitment to achieving universal access to reproductive health through expanding choice and method mix.”

– Marleen Temmerman, Director, Department of Reproductive Health and Research, World Health Organization (2013, European Union Caya launch)

Some product development stories end here, with a product approved by multiple regulating agencies, low-cost manufacturing established, and promotion to initial target audiences in select countries completed. But to reach women in low-income countries—who currently do not have access to a diaphragm—PATH and partners built evidence of the value proposition for this new method and created a roadmap for introduction. Health systems assessments, market research, and cost-effectiveness/health-impact modeling were implemented to describe characteristics of women likely to be interested in SILCS, how it can be introduced, and how it could improve women’s reproductive health—especially in countries with a limited contraceptive method mix and high unmet need for birth-spacing methods.

A family planning provider and researcher introduce SILCS to a former diaphragm user who had promoted diaphragms to her community decades ago when they were available.
Photo: PATH/Maggie Kilbourne-Brook

Assessing the health system fit

UGANDA

In 2010, researchers at Mbarara University of Science and Technology in Uganda implemented a health systems assessment to assess feasibility and opportunity for SILCS introduction. Potential users, providers, and policymakers recognized that the SILCS diaphragm could fill a gap in the method mix and expressed eagerness to make the SILCS diaphragm available, particularly because it is nonhormonal and woman-initiated. Stakeholders saw SILCS as a method that would increase choice and could improve women’s reproductive health in Uganda. Like many countries, Uganda’s family planning program is financially stretched, and clear support for the SILCS diaphragm by end users will need to be demonstrated before the product will be considered for public-sector introduction.

> “This one will be good, if it has no side effects. You will have saved us. We are tired of having children and yet we are young. The women here are desperate. Is there a woman who does not want family planning?”

– Rural woman, Mbarara

INDIA

From 2012 to 2013, researchers in India implemented a health systems assessment of feasibility and market opportunities for introduction of SILCS, and a market research firm implemented both quantitative and qualitative analyses to assess potential target markets. Findings identified a strong interest in SILCS as a contraceptive in India to expand the method mix to include a nonhormonal birth-spacing method. The political and policy environment is supportive of introducing this new method. Women from both urban and rural areas expressed interest in using SILCS. Despite being an unknown method, women indicated they could learn to use the diaphragm. Market research found that although awareness of the diaphragm is currently negligible, a diaphragm is attractive for young women who want control of family planning in their hands. If positioned and priced correctly, Caya could help address unmet need for family planning.

> “If you train us, we can properly insert SILCS after practice.”

– Female, Mysore

Scientists at the Division of Reproductive and Child Health, Indian Council of Medical Research provided input into the health systems assessment in India in 2012.
Photo: PATH/Maggie Kilbourne-Brook

SOUTH AFRICA

In 2014, Maternal, Adolescent and Child Health (MatCH) Research in Durban implemented a health systems assessment to assess opportunities and challenges for future introduction of the SILCS diaphragm in South Africa. This included a policy analysis, an assessment to determine health system readiness, and focus group discussions and interviews with potential consumers and providers. MatCH determined the policy environment is supportive for SILCS introduction, with a newly updated national contraceptive policy that mentions expanding the method mix. The regulatory process for SILCS as a contraceptive also is clear since SILCS is approved in Europe and the United States. The path for approval of a contraceptive gel is less clear, however, since currently there is not a contraceptive gel available in South Africa. Regulatory revisions are being discussed in South Africa that would make the medical device guidelines more similar to European guidelines, which could facilitate CayaGel approval once a local partner is found.

Stakeholders agreed there is need for nonhormonal alternatives for women who cannot use or want to avoid hormonal methods. SILCS was found acceptable for a range of women including urban and rural, married and single, and younger and older, and could provide an alternative when condoms cannot be used. Market research identified that Black women from middle- and lower-income groups were more interested in SILCS than higher-income women from other racial categories. And women were much more interested in using SILCS plus a microbicide gel together to protect from both pregnancy and HIV and other sexually transmitted infections (STIs) than in using SILCS just for contraception.

MatCH Research provided feedback about the Caya pelvic model during the health systems assessment in South Africa.
Photo: MatCH Research

Contraceptive gel

Across all three of these countries, a common challenge identified is ensuring access to a contraceptive gel for use with the diaphragm. Since the World Health Organization has recommended that products containing nonoxynol-9 not be used in countries where there is high risk of HIV, contraceptive gel has not been available in developing countries. For Caya diaphragm introduction to move forward, an alternative contraceptive gel that does not contain nonoxynol-9 must be available.

Kessel is currently assessing country partnerships in low-resource countries where the CE Mark and well-established safety of Contragel from decades of market experience are sufficient for registration. At the same time, CONRAD has implemented clinical studies to assess the safety and barrier effectiveness of SILCS used with Contragel. Data from these studies will supplement the Contragel/CayaGel regulatory dossier and could facilitate introduction in developing countries—even where women are at risk of HIV.

Photo: Kessel medintim GmbH

Evaluating the cost-effectiveness and potential health impact of SILCS

Health economists at the London School of Hygiene & Tropical Medicine built a model to estimate the impact and cost-effectiveness of introducing the SILCS diaphragm in Gauteng Province, South Africa, among women with unmet need for contraception. Results showed that at five years, the SILCS diaphragm could avert a total of 10,482 unintended pregnancies, which includes 2,217 abortions and 8,270 pregnancies that would have resulted in birth. SILCS diaphragm introduction could be cost-effective compared to other interventions for reducing unintended pregnancy. An additional cost-effectiveness and health-impact model has been developed that evaluates SILCS plus microbicide gel relative to other HIV prevention strategies that are or could be available in South Africa. This analysis identified that younger women—especially those not able to use condoms—prefer SILCS plus microbicide gel over other HIV prevention strategies such as oral PrEP (pre-exposure prophylaxis), the vaginal ring, and long-acting injectable ARVs, specifically because the combined product offers pregnancy prevention at the same time as HIV prevention.

SILCS as an MPT

In recent years, PATH and researcher partners have looked at ways to extend the health impact of SILCS by building evidence for using it to deliver HIV/STI protection.

Two MPT strategies have been proposed.

STRATEGY 1. The first strategy is to use SILCS as a reusable delivery system for microbicide gel. While no microbicide gel has yet demonstrated the effectiveness needed to lead to a regulatory submission, this seems due, in part, to the user regimen. New microbicide gels are in development that could be more effective and with simpler use regimens.

Clinical study results report that some women and men like using microbicide gel because it makes sex more pleasurable. If SILCS and microbicide gel can be promoted to couples who want user-initiated protection and like gel, this could be a winning scenario for pregnancy and HIV protection.

Three exploratory clinical studies suggest that using SILCS for microbicide gel delivery is feasible and acceptable for some couples. First, an MRI study implemented at the University of Pittsburgh found that gel delivered by SILCS covers the upper and lower vagina, similar to gel delivered by a vaginal applicator. Next, a study assessed acceptability of SILCS as a gel delivery system compared to a vaginal applicator for gel delivery and found that, while most participants in the United States preferred the applicator for its ease of use, most also thought SILCS plus gel would provide better protection from pregnancy and STIs than gel alone from an applicator. And they preferred SILCS for being less messy and having less gel leakage.

Among women in this study, 68 percent stated they would use SILCS plus microbicide gel as an MPT, compared to 17 percent of women who said they would use the SILCS diaphragm for contraception and 14 percent who said they would use an applicator and microbicide gel for HIV prevention.

This study was replicated in South Africa in 2014 and 2015 to collect data from a study population who perceived themselves to be more at risk of HIV. Data from this study, implemented by MatCH, found strong interest from both women and their partners in the SILCS diaphragm as a microbicide gel delivery system. Among women in this study, 68 percent stated they would use SILCS plus microbicide gel as an MPT, compared to 17 percent of women who said they would use the SILCS diaphragm for contraception and 14 percent who said they would use an applicator and microbicide gel for HIV prevention. This is an important signal that women want access to methods that can protect them from the multiple reproductive health risks they face.

Other studies also suggest that use of the diaphragm—which serves as a physical barrier protecting the cervix—can reduce risk of STIs that infect the cervix, such as gonorrhea, chlamydia, trichomoniasis, pelvic inflammatory disease, and human papillomavirus.

Kessel and PATH have worked with microbicide gel product developers such as CONRAD and the Population Council to include SILCS as a delivery system for microbicide gel in the development path for their products.

STRATEGY 2. The second MPT strategy involves a modified SILCS spring loaded with an ARV drug, such as dapivirine,* which would allow SILCS to become a controlled-release delivery system for an ARV for HIV prevention. This strategy has been tested through proof-of-concept. In vitro testing has been shown to deliver drug release at protective levels for up to one year, or possibly longer. PATH and research partners at Queens University Belfast are seeking funding to continue development of SILCS for this MPT indication.

Demonstrating the Caya diahragm at a midwifery conference in France.
Photo: Kessel medintim GmbH

* Dapivirine is an ARV developed by Janssen Sciences Ireland UC, and licensed to the International Partnership for Microbicides for use as a microbicide in resource-poor countries.

> “This woman-initiated, nonhormonal contraceptive barrier method could serve as a delivery method for gels that help protect against HIV and other sexually transmitted infections—it could be our first true multipurpose prevention product.”
>
> – Judy Manning, team lead for contraceptive research and development at USAID (2015)

SILCS Completed

THE CAYA STORY CONTINUES

> “The Caya diaphragm is an important step toward introducing diaphragms to a new generation of women who may never have seen or heard of this method.”
>
> – Martin Kessel, CEO, Kessel medintim GmbH

PATH is grateful to the partners and supporters who helped develop and bring to market this new contraceptive device that expands women’s reproductive health options. Already, Caya introduction is reinvigorating interest in female barrier methods as a new generation of women in developed and middle-income countries learn about the diaphragm. PATH’s funded work building evidence and launching this new diaphragm comes to a close in 2016. Yet the story will continue, as Kessel and new partners introduce the Caya diaphragm to women in low-resource settings.

For Caya to achieve impact by providing a nonhormonal option in low-resource settings, both private- and public-sector support will be needed. Partners such as the USAID-funded Expanding Effective Contraceptive Options project have already incorporated Caya into the basket of woman-initiated methods being introduced to address unmet need for family planning. And Kessel is working with NGOs and social-marketing groups to assess interest in and next steps for introduction. For example, health care providers in Nigeria have expressed strong interest in Caya as a method that could provide a nonhormonal option for young women in that country. This reinforces Kessel’s commitment to seeking partnerships to expand access in low-resource countries.

> “This visit [to Nigeria] was like reaching a goal, [one] that was a long time visible, but still far away. Now, we know that Caya is a method for a lot more women than Europeans or North Americans.”
>
> – Martin Kessel (2016)

While Kessel and partners move forward introducing Caya in developed and developing countries as a contraceptive, building evidence for SILCS as an MPT will leverage the existing investment and generate additional health benefit from this new nonhormonal method.

The circle of Caya supporters and partners is growing as policymakers, researchers, NGO partners, family planning providers, and private-sector distributors learn about the Caya diaphragm. Now led by Kessel, the Caya diaphragm is on the move as partners explore how to introduce and build markets for Caya as a product that expands reproductive health options for women.

Photo: PATH/Patrick McKern

Photo: MatCH Research Unit

Resources

Caya Europe: **http://www.caya.eu/en/**

Caya United States: **http://caya.us.com/**

Technologies for Reproductive Health **http://sites.path.org/rhtech/silcs-diaphragm/**

- SILCS overview
- Summary of clinical studies
- SILCS as an MPT
- SILCS policy brief for South Africa

Cervical Barrier Advancement Society: **http://www.cervicalbarriers.org/**

Yahoo.com user group for women considering using diaphragm and cervical caps: **https://groups.yahoo.com/neo/groups/DiaphragmsAndCaps/info**

SILCS Publications List (as of 2015)

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Schwartz J, Mauck C, Rountree W, Ballagh S, Crenin M, Kilbourne-Brook M. SILCS diaphragm: postcoital testing of a new single-size contraceptive diaphragm. *Obstetrics & Gynecology*. 2006;107:S12.

> "... diaphragms are included on the World Health Organization Model List of Essential Medicines, this makes it astonishing that so many people have difficulty locating a diaphragm... Should access to a diaphragm be considered a right?"
>
> – May 29, DiaphragmAndCaps discussion board

SILCS Partners

Funders

USAID, Office of Population and Reproductive Health and Office of HIV/AIDS
The Bill & Melinda Gates Foundation
The Andrew W. Mellon Foundation
The William and Flora Hewlett Foundation

Clinical research and regulatory partner

CONRAD, Arlington Virginia USA, and the CONRAD clinical trials network:
Eastern Virginia Medical School, California Family Health Council, University of Pittsburgh, Johns Hopkins Community Physicians, University of Pennsylvania, Baylor College of Medicine, FHI 360; Profamilia Biomedical Research Department

Seattle, Washington USA

Aurora Medical Services
Planned Parenthood Greater Seattle
Seattle Midwifery School
University of Washington, Departments of Urology and Radiology

Dominican Republic, South Africa, and Thailand

Profamilia, Biomedical Research Department, Dominican Republic
Maternal, Adolescent and Child Health (MatCH) Research Unit, South Africa
Khon Kaen University, Department of Medical Surgical Nursing, Faculty of Nursing, Thailand

Zimbabwe

Women's Global Health Imperative, RTI International, and the Center for AIDS Prevention Studies University of California San Francisco, Department of Medicine
University of Zimbabwe/University of California San Francisco Collaborative Research Program in Women's Health

Manufacturing

SILCS, Inc., New Jersey USA
Molded Rubber Plastics Corporation (MPRC), Wisconsin USA
Kessel medintim GmbH, Germany

SILCS as an MPT

University of Pennsylvania
The Miriam Hospital/Alpert Medical School of Brown University
ReProtect, Inc.
California Family Health Council
Queens University Belfast, School of Pharmacy
International Partnership for Microbicides
The Population Council
London School of Hygiene & Tropical Medicine, Global Health and Development Department, University of Bristol

Health systems assessments and market research in India, South Africa, and Uganda

Ashodaya Samithi, India; Katharine Shapiro, independent consultant; and IMRB International, India
MatCH Research and Added Value, South Africa
Mbarara University of Science and Technology, Uganda

USAID
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